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Analysis of characteristics and prognosis of *multi-drug resistant Pseudomonas aeruginosa* pulmonary infection in elderly patients

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Abstract: This study aimed to analyze the characteristics and prognostic factors of *multi-drug resistant Pseudomonas aeruginosa* (*MDRPA*) pulmonary infection in elderly patients. Clinical data from 118 elderly patients diagnosed with *MDRPA* infections at Chinese PLA General Hospital were retrospectively reviewed. The 118 cases were mainly from ICU (51 cases, 43.22%) and respiratory department (30 cases, 25.42%). Among *MDRPA* strains isolated, resistance rates were highest for aztreonam (79.66%), ticarcillin (59.32%), and piperacillin (53.39%), and lowest for tobramycin (15.25%), amikacin (16.49%), and gentamicin (19.49%). ROC analysis highlighted ICU admission (AUC=0.718, sensitivity=73.8%, specificity=69.7%) as the strongest predictor. Logistic regression analysis showed that age ≥68.5 years (P=0.022, OR=6.907, 95%CI:1.320-36.152), history of diabetes and cardiovascular disease (P=0.005, OR=4.147, 95%CI:1.526-11.274; P=0.009, OR=3.702, 95%CI:1.387-9.884) and admission to ICU (P<0.001, OR=8.097, 95%CI:3.031-21.635) were independent predictors of poor prognosis in elderly patients with *MDRPA* pulmonary infection. The primary departments responsible for *MDRPA* pulmonary infections in elderly patients were the ICU and the Respiratory Department. The resistance situation was severe, particularly for aztreonam, ticarcillin and piperacillin. Admission to ICU was a significant predictor of poor prognosis, while age, history of diabetes and cardiovascular diseases also had a notable impact on prognosis.

Keywords: Multi-drug resistant *Pseudomonas aeruginosa*; elderly patients; pulmonary infection; characteristics; prognosis

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INTRODUCTION

Pseudomonas aeruginosa (*PA*) is one of the most common opportunistic pathogens in clinical practice and its wide natural distribution and strong environmental adaptability make it an important pathogen causing nosocomial infections(Reynolds D and Kollef M 2021). In elderly patients, the infection rate of *Pseudomonas aeruginosa* increases significantly due to the natural decline of the immune system, the combination of multiple chronic diseases and frequent medical interventions (Goto A, *et al.*, 2023). With the wide application of broad-spectrum antibiotics, the problem of drug resistance of *Pseudomonas aeruginosa* has become increasingly serious. The emergence of Multi-drug resistant (MDR) strains has greatly challenged the existing clinical treatment plan (Zhu Y, *et al.*, 2022). *Multi-drug resistant Pseudomonas aeruginosa* (*MDRPA*) refers to strains that are resistant to a variety of antibacterial drugs with different mechanisms or structures at the same time. Elderly patients are at high risk of *MDRPA* infection due to the decline of physical function, slow drug metabolism and the need for long-term or repeated use of antibiotics (Yin C, *et al.*, 2024; Tang S, *et al.*, 2024). *MDRPA* pulmonary infection not only has a long course of disease and serious condition, but also is difficult to treat, which often leads to poor prognosis of patients, increased hospitalization days and medical costs and even life-threatening in severe cases (Adelantado, *et al.*, 2022).Therefore, in-depth study of the characteristics and prognosis evaluation of *MDRPA* pulmonary infection in elderly patients holds immense importance in directing clinically appropriate medication use and enhancing patient outcomes (Pulmonary Infection Assembly of Chinese Thoracic Society, 2022). Currently, limited research exists concerning the characteristics and assessment of the prognosis for elderly patients suffering from *MDRPA* pulmonary infection. Consequently, this study intends to investigate the clinical characteristics of elderly patients with *MDRPA* pulmonary infection, analyze the characteristics, epidemic trend and drug resistance of *MDRPA* and provide guidance for clinical medication. Simultaneously, the prognosis of elderly individuals suffering from *MDRPA* pulmonary infection was assessed and the primary factors influencing their outcome were explored, aiming to offer novel insights and approaches to decrease the incidence of unfavorable prognoses in this patient population.

MATERIALS AND METHODS

Study design and participants

This study was a retrospective study to analyze the

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characteristics and prognostic factors of elderly patients with *MDRPA* pulmonary infection. The subjects of this study were 118 elderly patients with *MDRPA* isolated from sputum samples in our hospital from January 2022 to December 2023 and diagnosed with pulmonary infection. The homogeneity of the subjects and the reliability of the data were ensured by clear inclusion and exclusion criteria. This study has been reviewed and approved by the Chinese PLA General Hospital ethics committee.

Inclusion criteria: (1) aged ≥ 60 years old; (2) meet the diagnostic criteria of pulmonary infection(Pulmonary Infection Assembly of Chinese Thoracic Society, 2022), sputum culture at least once showed *Pseudomonas aeruginosa*; (3) in accordance with the diagnostic criteria of multidrug resistance (Paul M, *et al*., 2022); (4) Patients were hospitalized in our hospital and had complete clinical data. Exclusion criteria: (1) pulmonary infection caused by other pathogens or mixed infection; (2) patients with immune system diseases; (3) patients with pulmonary diseases such as tuberculosis, pulmonary fibrosis, pulmonary edema and pulmonary embolism.

METHODS

We gathered the clinical information of the patients through our hospital's medical record inquiry system, encompassing age, gender, history of hypertension, diabetes, COPD, brain and nervous system diseases, cardiovascular system diseases, tumors, smoking history, drinking history, invasive operation (artificial airway, mechanical ventilation, etc.), admission to ICU and surgical treatment. At the same time, the related information of *MDRPA* was collected, including the source department and the results of drug susceptibility test. The drug susceptibility test was performed according to the 2015 clinical and laboratory standards institute (CISI) standard. Kirby-Bauer disk AGAR diffusion method was used to detect the drug resistance of *Pseudomonas aeruginosa* to 13 kinds of antibiotics and 7 kinds of common clinical antibiotics. Including aminoglycosides (amikacin, gentamicin, tobramycin), cephalosporins (ceftazidime, cefepime), penicillins (piperacillin, ticarcillin), carbapenems (imipenem, meropenem), β-lactamase inhibitor complex (peracillin/tazobactam), monocyclic β-lactams (aztreonam), fluoroquinolones (ciprofloxacin) and levofloxacin). PA were classified as susceptible (S), intermediate (I) and resistant (R) according to their susceptibility to antimicrobial agents. *Multidrug-resistant Pseudomonas aeruginosa* (*MDRPA*) was defined as drug resistance to 3 or more than 3 of the above 7 classes (not three in the same class)(de Almeida,et al., 2017).

Prognostic indicators

According to the final outcome of elderly patients with *MDRPA* pulmonary infection, they were categorized into the good prognosis group (n=76) who showed improvement and were discharged and the poor prognosis group (n=42) who died. An analysis was then conducted to identify the factors influencing the prognosis of elderly patients with *MDRPA* pulmonary infection, using the clinical data from both groups.

Ethic approval

The study was approved by Ethics Committee of the Chinese PLA General Hospital (approval number: S2023-061-01).

STATISTICAL ANALYSIS

The data were analyzed using SPSS 26.0. For count data, the representation was n (%), whereas measurement data adhering to normal distribution were detailed as (`x±s). The differences between the poor prognosis and the good prognosis groups were compared by χ^2 test and the ROC curve was employed to assess the predictive efficacy of *MDRPA* pulmonary infection related indicators for the prognosis of patients. Logistic regression analysis was utilized to identify the factors affecting the prognosis of *MDRPA* pulmonary infection in elderly patients, with statistical significance set at $P<0.05$.

RESULTS

Clinical data of the study subjects

A total of 118 elderly patients with *MDRPA* pulmonary infection were enrolled in this study. The age ranged from 60 to 88 years, with an average age of (74.27±6.28) years, including 71 males (60.17%) and 44 females (37.29%). Details of the patient's past medical history and other clinical data are provided in table 1.

Distribution of the source departments of MDRPA pulmonary infection in elderly patients

The 118 cases were mainly from 6 departments, mainly from ICU (51 cases, 43.22%). Followed by respiratory department 30 cases (25.42%), neurosurgery 9 cases (7.63%), oncology 9 cases (7.63%), thoracic surgery 7 cases (5.93%) 7 cases (5.93%) from Department of Neurology and 5 cases (4.24%) from other departments (2 cases from department of infection, 1 case from Department of nephrology, 1 case from department of endocrinology and 1 case from department of Gastroenterology). See table 2.

Analysis of MDRPA resistance in elderly patients

The resistance of *MDRPA* strains from 118 elderly patients to 13 antimicrobial agents is shown in table 3, fig. 1. *MDRPA* strains resistant to 4,5 and 6 antibiotics were the most, with 27 cases in each group. *MDRPA* strains with 8 antibiotic resistance were the least, with a total of 3 cases (fig. 1). Among 118 *MDRPA* strains isolated from elderly patients, aztreonam had the highest resistance rate (79.66%), followed by ticarcillin (59.32%) and piperacillin

Table 1: Clinical data of the study subjects

Items	Number of people (cases)	Percentage (%)
Sex		
Female	44	37.29
Male	71	60.17
Hypertension		
No	75	63.56
Yes	43	36.44
Diabetes		
No	82	69.49
Yes	36	30.51
COPD		
No	101	85.59
Yes	17	14.41
Brain and nervous system diseases		
No	99	83.90
Yes	19	16.10
Cardiovascular diseases		
No	78	66.10
Yes	40	33.90
Undergo surgical treatment		
No	73	61.86
Yes	45	38.14
Tumors		
No	109	92.37
Yes	9	7.63
Invasive Procedures		
No	84	71.19
Yes	34	28.81
History of smoking		
No	91	77.12
Yes	27	22.88
History of drinking		
No	92	77.97
Yes	26	22.03
Admission to ICU		
No	64	54.24
Yes	54	45.76

Table 2: Distribution of the source departments of *MDRPA* pulmonary infection in elderly patients

Department of Infectious Diseases	Number of people (cases)	Percentage (%)
ICU	51	43.22
Department of respiratory	30	25.42
Neurosurgery	9	7.63
Department of Neurology	7	5.93
Thoracic	7	5.93
Oncology	9	7.63
Other Department	5	4.24

(53.39%) and the resistance rate was more than 50%. The lowest resistance rate was tobramycin (15.25%), followed by amikacin (16.49%) and gentamicin (19.49%), all of which were less than 20% (table 3).

Univariate analysis of the prognosis of MDRPA pulmonary infection in elderly patients

Based on their prognosis, 118 elderly patients suffering from *MDRPA* pulmonary infection were categorized into the good prognosis group (76 cases) and the poor prognosis group (42 cases). Age as a continuous variable was divided into binary variables according to the best cut-off value of ROC curve and the general data of the two groups of patients were analyzed by univariate analysis. Univariate analysis was conducted on the general data of both groups. The findings revealed statistically significant disparities between the two groups in terms of age, diabetes, cardiovascular disease and admission to ICU (P=0.009; P=0.001; P=0.002; P<0.001) (table 4).

Table 3: *MDRPA* resistance [n(%)]

Antimicrobial agents	Susceptible (S)	Intermediate (I)	Resistant (R)
Cephalosporins			
Ceftazidime	33(27.97)	32(27.12)	53(44.91)
Cefepime	27(22.88)	41(34.75)	50(42.37)
Monocyclic β-lactams			
Aztreonam	3(2.54)	21(17.80)	94(79.66)
Penicillins			
Piperacillin	19(16.10)	36(30.51)	63(53.39)
Ticarcillin	14(11.86)	34(28.81)	70(59.32)
β-lactamase inhibitor compound agent			
Piperacillin sodium/tazobactam sodium	13(11.02)	70(59.32)	35(29.66)
Carbapenems			
Meropenem	49(41.53)	45(38.14)	24(20.34)
Imipenem	47(39.83)	41(34.75)	30(25.42)
Quinolone			
Ciprofloxacin	30(25.42)	50(42.37)	38(32.20)
Levofloxacin	33(27.97)	40(33.90)	45(38.14)
Aminoglycosides			
Gentamycin	50(42.37)	45(38.14)	23(19.49)
Tobramycin	70(59.32)	30(25.42)	18(15.25)
Amikacin	76(64.41)	22(18.64)	20(16.49)

Table 4: Univariate analysis of the prognosis of *MDRPA* pulmonary infection in elderly patients

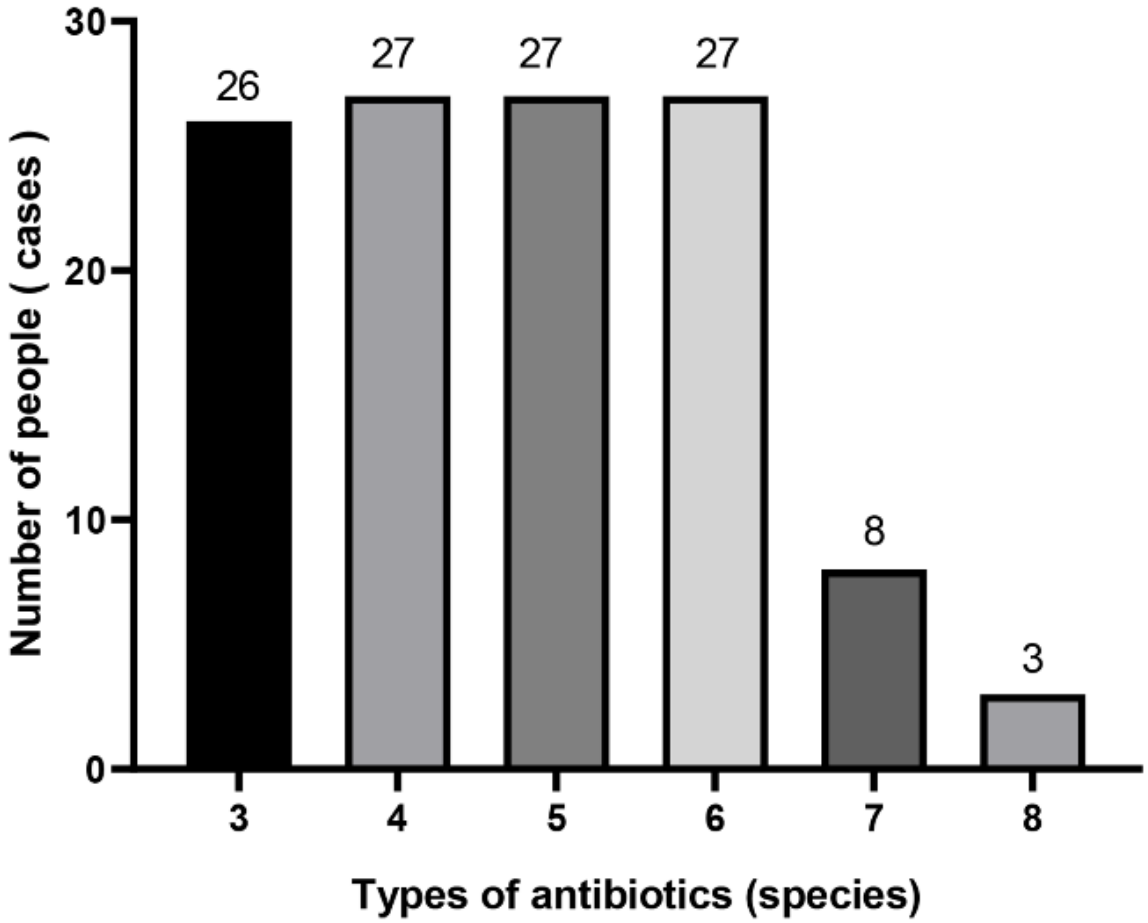
Factors	Good prognosis group (n=76)	Poor prognosis group (n=42)	χ^2	*P*
Age [n(%)]			6.881	0.009
≥68.5 years	58(76.32)	40(95.24)		
<68.5years	18(23.68)	2(4.76)		
Sex [n(%)]			0.865	0.352
Female	26(34.21)	18(42.86)		
Male	50(65.79)	24(57.14)		
Hypertension [n(%)]			1.159	0.282
No	51(67.11)	24(57.14)		
Yes	25(32.89)	18(42.86)		
Diabetes [n(%)]			11.686	0.001
No	61(80.26)	21(50.00)		
Yes	15(19.74)	21(50.00)		
COPD [n(%)]			0.270	0.603
No	66(86.84)	35(83.33)		
Yes	10(13.16)	7(16.67)		
Brain and nervous system diseases [n(%)]			0.159	0.690
No	63(82.89)	36(85.71)		
Yes	13(17.11)	6(14.29)		
Cardiovascular diseases [n(%)]			9.942	0.002
No	58(76.32)	20(47.62)		
Yes	18(23.68)	22(52.38)		
Undergo surgical treatment [n(%)]			2.486	0.115
No	51(67.10)	22(52.38)		
Yes	25(32.89)	20(47.62)		
Tumors [n(%)]			0.022	0.883
No	70(92.11)	39(92.86)		
Yes	6(7.89)	3(7.14)		
Invasive Procedures [n(%)]			0.796	0.372
No	52(68.42)	32(76.19)		
Yes	24(31.58)	10(23.81)		
History of smoking [n(%)]			0.405	0.525
No	60(78.95)	31(73.81)		
Yes	16(21.05)	11(26.19)		
History of drinking [n(%)]			1.622	0.203
No	62(81.58)	30(71.43)		
Yes	14(18.42)	12(28.57)		
Admission to ICU [n(%)]			20.667	<0.001
No	53(69.74)	11(26.19)		
Yes	23(30.26)	31(73.81)		

Table 5: Evaluation value of *MDRPA* pulmonary infection-related indicators on prognosis of elderly patients

Indicators	AUC	95%*CI*	Sensitivity (%)	Specificity (%)
Age	0.595	0.492~0.697	95.2	23.7
Diabetes	0.651	0.544~0.758	50.0	80.3
Cardiovascular disease	0.643	0.537~0.750	52.4	76.3
Admission to ICU	0.718	0.620~0.815	73.8	69.7

Table 6: Logistic regression analysis of the prognosis of *MDRPA* pulmonary infection in elderly patients

Variables	*β*	*S.E*	*P*	*OR*	*95%CI*
Age	2.207	0.837	0.022	6.907	1.320~36.152
Diabetes	0.995	0.492	0.005	4.147	1.526~11.274
Cardiovascular diseases	1.027	0.476	0.009	3.702	1.387~9.884
Admission to ICU	1.922	0.475	<0.001	8.097	3.031~21.635



Note: The abscissa indicates how many kinds of antibiotic are coresistant in a patient (i.e., the 13 antibiotics for which susceptibility testing was performed), and the ordinate indicates how many patients are resistant to that specific number of antibiotics.

Fig. 1: Distribution of *MDRPA* in the number of antibiotic resistance

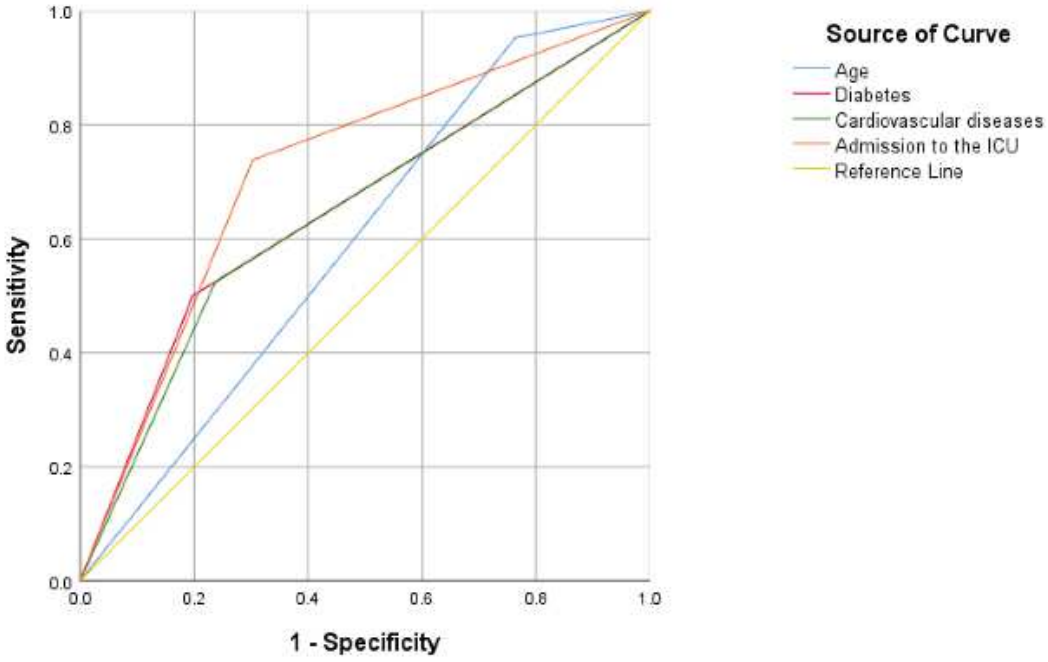


Fig. 2: ROC curve of *MDRPA* pulmonary infection related indicators to evaluate the prognosis of elderly patients

Evaluation value of MDRPA pulmonary infection-related indicators on prognosis of elderly patients

The predictive value of factors such as age, diabetes, cardiovascular disease and admission to ICU for the prognosis of *MDRPA* pulmonary infection in elderly patients was assessed using a Receiver Operating Characteristic (ROC) curve. Among these factors, admission to ICU exhibited the highest Area Under the Curve (AUC) value of 0.718, accompanied by a sensitivity of 73.8% and a specificity of 69.7%. Diabetes followed with an AUC of 0.651, sensitivity of 50.0% and specificity of 80.3%. Cardiovascular disease had an AUC of 0.643, sensitivity of 52.4% and specificity of 76.3%. Lastly, age showed an AUC of 0.595, with a high sensitivity of 95.2% but a relatively low specificity of 23.7% (table 5 and fig. 2).

Logistic regression analysis of the prognosis of MDRPA pulmonary infection in elderly patients

Whether the elderly patients had a good prognosis (good prognosis =0, poor prognosis =1) was used as the dependent variable and statistically significant variables in the univariate analysis. The assignment is as follows: age (1=≥68.5 years old, 0=<68.5 years old), diabetes (1= Yes, 0= No), cardiovascular disease (1= Yes, 0= No), Admission to ICU (1= Yes, 0= No). Logistic regression analysis showed that age ≥68.5 years old (P=0.022, OR=6.907, 95%CI: 1.320-36.152), history of diabetes and cardiovascular disease (P=0.005, OR=4.147, 95%CI: 1.526-11.274; P=0.009, OR=3.702, 95%CI: 1.387-9.884) and admission to ICU (P<0.001, OR=8.097, 95%CI: 3.031-21.635) were independent predictors of poor prognosis in elderly patients with *MDRPA* pulmonary infection (table 6).

DISCUSSION

Among 118 elderly patients with *MDRPA* pulmonary infection in our hospital, ICU was the main infection source department, accounting for 43.22%, which was significantly higher than other departments, indicating that ICU was the high incidence area of *MDRPA* pulmonary infection in elderly patients, which was similar to previous research results (Kresken, *et al*., 2020). ICU is an intensive care area and the elderly patients in ICU have critical condition, low immune function and frequent invasive operations such as prolonged bed rest, mechanical ventilation and indwelling catheter, which together increase the risk of *MDRPA* infection. Elderly patients in ICU are often treated with multiple antibiotics, which may not only lead to flora imbalance, but also promote the selective growth of *MDRPA* and the development of drug resistance (Brunke, *et al.*, 2023; Ibrahim, *et al.*, 2024). In addition, *MDRPA* pulmonary infection cases have also been found in other departments, suggesting that *MDRPA* infection is not limited to high-risk departments in the traditional sense, but should attract the attention of the whole hospital (Van, *et al*., 2023).

In this study, *MDRPA* strains showed extensive resistance to a variety of antibiotics, especially the resistance rate of aztreonam, ticarcillin and piperacillin exceeded 50%, which was similar to the results of previous studies (Nasrin S, *et al.*, 2022; Kiyaga S, *et al.*, 2022; Pan D, *et al.*, 2022). This may be related to the widespread use of these drugs in clinical practice and non-standard medication habits, leading to the selective resistance of *MDRPA* strains. Aztreonam, a monocyclic β-lactam antibiotic, plays an antibacterial role mainly by inhibiting the synthesis of bacterial cell wall. However, *MDRPA* can hydrolyze aztreonam by producing β-lactamase, thus losing its antibacterial activity. As penicillins, the resistance mechanism of ticarcillin and piperacillin may be related to penicillinase produced by bacteria (Assefa M 2022). In contrast, the low rates of resistance to tobramycin, amikacin and gentamicin may be related to the less frequent use of these agents at this hospital or to clinicians' preference to preserve susceptibility to these agents when selecting antibiotics. When compared to previous research findings, the resistance rates of *MDRPA* observed in this study exhibited variations, which could potentially be attributed to diverse factors such as different hospitals and different regions' antibiotic use habits, pathogen prevalence, patients' basic diseases and immune function status (Kalın G, *et al*., 2023). Therefore, in clinical practice, antibiotics should be selected reasonably according to the drug resistance of local pathogens, the specific conditions of patients and the sensitivity test results of drugs, so as to avoid abuse and reduce the generation and spread of *MDRPA* (Theodorakis, *et al*., 2024).

Univariate analysis revealed statistically significant differences in age, diabetes, cardiovascular disease and admission to ICU between the two groups, suggests that these factors potentially playing a crucial role in determining the prognosis of elderly patients suffering from *MDRPA* pulmonary infection. The ROC curve was used to evaluate the predictive efficacy of these factors and we found that admission to ICU had the highest predictive value, with an AUC of 0.718, which had high sensitivity and specificity. This suggests that admission to ICU can be used as one of the important indicators to predict the prognosis of *MDRPA* pulmonary infection in elderly patients (Raman G, *et al*., 2018). The predictive value of diabetes and cardiovascular system diseases is the second, but it still has certain clinical reference value. In contrast, the predictive value of age is relatively low, which may be related to the common characteristics of older age and decreased physiological function in elderly patients, making the effect of age on prognosis relatively complicated.

Further, Logistic regression analysis was used to identify the independent predictive factors for the prognosis of *MDRPA* pulmonary infection in elderly patients, including age, diabetes, cardiovascular system diseases and admission to ICU. Age ≥68.5 years was an independent predictor of poor prognosis in elderly patients with *MDRPA* pulmonary infection (P=0.022, OR=6.907), which was similar to the results of Yin *et al* (Yin, *et al*., 2021). It is suggested that with the increase of age, the physiological function of the elderly patients is gradually declining, the function of the immune system is decreased and the resistance and recovery ability to infection are weakened, which increases the risk of death after pulmonary infection. In addition, elderly patients have limited physiological reserve and may have poor responsiveness and tolerance to drug treatment, further increasing the risk of poor prognosis (Zhou C, *et al*., 2023). Therefore, more attention should be paid to early intervention and comprehensive treatment to reduce the incidence of poor prognosis in elderly patients with *MDRPA* pulmonary infection.α The results of this study showed that elderly patients with previous diabetes (P=0.005, OR=4.147) and cardiovascular diseases (P=0.009, OR=3.702) had a significantly increased risk of poor prognosis of *MDRPA* pulmonary infection, which was similar to the results of previous studies (Hernández-Jiménez, *et al.*, 2022; Zhang Y, *et al.*, 2020). Due to the elevated blood glucose level and impaired immune function, diabetic patients are prone to complicated infection and infection is difficult to control (Zhang S, *et al*., 2023). Patients with cardiovascular diseases may have problems such as decreased cardiopulmonary function and blood circulation disorders, which are prone to rapid deterioration after pulmonary infection (Respiratory Branch of Chinese Geriatrics Society 2025). These underlying diseases not only increase the risk of pulmonary infection in elderly patients, but also significantly affect their prognosis.β The risk of poor prognosis of *MDRPA* pulmonary infection in elderly patients admitted to ICU was significantly increased (P<0.001, OR=8.097), which was consistent with previous studies (Raman G, *et al*., 2018). Admission to ICU usually means that patients are in critical condition and need advanced life support and close monitoring. These patients often have complex conditions such as multiple organ failure and severe infection and have poor responsiveness and tolerance to treatment. In addition, the risk of cross infection in the ICU environment is also high, which may further aggravates the infection condition of patients (Wang Z, *et al*., 2018). Therefore, in view of these risk factors, clinicians should formulate personalized treatment plans, strengthen the management and control of underlying diseases and optimize the ICU environment to reduce the risk of death in elderly patients with *MDRPA* pulmonary infection (Ibrahim K, *et al*., 2024).

This study also has certain limitations. This study is a single-center study with relatively small sample size and enrolled patients in the same hospital, which may not reflect the drug resistance of pathogens in other hospitals or regions and the specific risk factors of patients. Data collected retrospectively may be subject to incomplete information or inaccurate records, which may bias sample

selection and limit the generalizability of the results. Therefore, multi-center prospective studies can be carried out in the future to expand the sample size and improve the representativeness and reliability of the results. At the same time, a standardized data collection process was adopted to ensure the completeness and accuracy of the data (Kang, *et al*., 2021).

CONCLUSION

The primary departments responsible for *MDRPA* pulmonary infections in elderly patients were the ICU and the Respiratory Department. The resistance situation was severe, particularly for aztreonam, ticarcillin and piperacillin. Admission to ICU was a significant predictor of poor prognosis, while age, history of diabetes and cardiovascular diseases also had a notable impact on prognosis. Therefore, for elderly patients with *MDRPA* pulmonary infection, we should pay attention to the management of high risk factors and strengthen the rational use of antibiotics, so as to improve the therapeutic effect and reduce the risk of poor prognosis in elderly patients.

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Author's contribution
Geping Qu, Zhiyan Wang, These are co-first authors, and they contributed to this work equally.

Consent to publish
The manuscript has neither been previously published nor is under consideration by any other journal. The authors have all approved the content of the paper.

Consent to participate
We secured a signed informed consent form from every participant.

Conflict of interest
There is no conflict of interest.

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