Infection and Drug Resistance

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ORIGINAL RESEARCH

Evaluation of the Efficacy of a Nomogram to Predict Multidrug-Resistant Pulmonary Infections Based on Data from Neurosurgery Ward Patients

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Objective: This study aimed to construct and evaluate a nomogram based on data from neurosurgery ward patients to predict the probability of multidrug-resistant (MDR) pneumonia occurrence.

Methods: We retrospectively collected clinical data, early laboratory test results, and physician prescriptions for 35 variables from patients. Univariate and stepwise regression analyses were used to screen variables to determine predictive factors, and a nomogram was constructed in the training group based on the results of the logistic regression model. Using the validation group, discrimination, calibration, and clinical applicability were assessed based on the receiver operating characteristic curve, calibration curve, and decision curve analysis (DCA).

Results: Among 3397 patients admitted to the neurosurgery ward from January 1, 2021, to September 30, 2024, 438 patients had pulmonary infections, including 208 patients with MDR pneumonia and 230 patients with non-MDR pneumonia. We randomly divided these patients into a training group (70%, N = 307) and a validation group (30%, N = 131). The nomogram consisted of only six predictive factors (creatinine clearance rate (CCR)≥130 mL/min/1.73 m^2, the Day 1 neutrophil-to-lymphocyte ratio (NLR), albumin≤30 g/L, hemoglobin, combination of antibacterial drugs, and tracheostomy), which demonstrated significantly higher sensitivity and specificity in the early identification of MDR pneumonia (AUC of the training group = 0.816 (95% CI: 0.760–0.862), AUC of the validation group = 0.797 (95% CI: 0.720–0.874)) and good calibration. DCA confirmed the clinical applicability of this nomogram.

Conclusion: We propose for the first time that augmented renal clearance (ARC) is an independent risk factor for the occurrence of MDR pneumonia in neurosurgical patients. Moreover, we successfully established a convenient prediction model that consists of six prediction factors, which can assist neurosurgeons in making early predictions of the incidence of MDR pneumonia.

Keywords: pulmonary infections, multidrug-resistant, nomogram, early diagnosis, neurosurgery ward

Introduction

Due to severe damage to the central nervous system, neurosurgical patients may experience swallowing dysfunction, consciousness disorders, and impaired protective airway reflexes. Additionally, patients frequently undergo various invasive procedures during treatment, such as tracheal intubation, mechanical ventilation, and central venous catheterization, creating conditions for bacterial invasion and hospital infections.[1] Moreover, due to autonomic nervous dysfunction and hypothalamic dysfunction in patients, the body's resistance decreases, further increasing the risk of infection.[2] Among the many challenges faced in the field of neurosurgery, hospital infection is an important and

Received: 9 April 2025
Accepted: 20 July 2025
Published: 26 July 2025

potentially reversible risk factor. Particularly in the lungs, the incidence can reach as high as 50%, severely affecting patient prognosis.[3]

Antibiotic resistance has become an extremely severe and urgent public health issue globally. With the widespread use of antimicrobial drugs, bacteria continuously evolve various resistance mechanisms, leading to a gradual decrease in the efficacy of traditional antimicrobial drugs and even resistance. Multidrug resistance (MDR) refers to acquired insensitivity to at least one drug in each of three or more classes of antimicrobial drugs.[4,5] MDR pulmonary infections can result in prolonged hospital stays, increased hospitalization costs, and an attributable mortality rate as high as 38.9–60.0%.[6] Early identification of high-risk populations for MDR pneumonia in neurosurgery wards is particularly important for improving patient prognosis.

Nomograms, an intuitive and individualized predictive tool, help identify high-risk patients via the recognition of risk factors, assisting treatment teams in making better clinical decisions. They have been widely studied in diseases such as pediatric biliary atresia, hemangioma, and delirium.[7–9]

Therefore, we investigated the current state of secondary pulmonary infections in neurosurgery ward patients and explored the risk factors for MDR pneumonia. By constructing a nomogram prediction model, we aimed to provide a convenient and accurate predictive tool for clinical use, with the goal of offering a reference for the early diagnosis and prevention of high-risk populations for MDR pneumonia in the neurosurgery ward.

Materials and Methods

Patient Recruitment

This study included patients admitted to the neurosurgery ward of the First Affiliated Hospital of the University of Science and Technology of China from January 1, 2021, to September 30, 2024. Patients were excluded if they were diagnosed with pneumonia before admission to the neurosurgery ward or within 48 hours of admission, if they had no pulmonary infection, or if their medical records were incomplete. Patients were divided into the "MDR pneumonia group" and the "non-MDR pneumonia group".

Definition of MDR

Acquired nonsensitivity to at least one drug in each of the three or more classes of antimicrobial agents. Definition of extensively drug-resistant (XDR): Resistance to all other classes of antimicrobial agents except for Classes 1–2. Definition of pandrug resistance (PDR): Nonsensitivity to any drug in all categories of antimicrobial agents.[4,5] Therefore, MDR also includes XDR and PDR.

The diagnosis of pneumonia follows the pneumonia diagnostic criteria jointly established by the American Society of Infectious Diseases and the American Thoracic Society in 2007 and the "Guidelines for the Diagnosis and Treatment of Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia in Adults (2018 Edition)": Chest X-ray or CT shows newly developed or progressive infiltrative, consolidative, or ground–glass opacities, plus at least two of the following three clinical symptoms: (1) fever, body temperature >38 °C; (2) purulent airway secretions; and (3) peripheral blood leukocyte count $>10\times10^9$/L or $<4\times10^9$/L.[10,11] Moreover, patients with conditions such as pulmonary embolism, pulmonary hemorrhage, pulmonary edema, acute respiratory distress syndrome, pulmonary vasculitis, pulmonary tumors, and radiation pneumonia were excluded. This study did not separately model hospital-acquired pneumonia and ventilator-associated pneumonia to reduce errors caused by differences in diagnostic criteria and to expand the applicability of the model.

Pathogen Diagnosis

The collected respiratory samples included deep sputum from the patient, endotracheal aspirate (ETA), bronchoalveolar lavage fluid (BALF), and protected specimen brush (PSB). A qualified respiratory specimen was defined as having fewer than 10 epithelial cells and more than 25 white blood cells per microscopic field. Furthermore, a qualified specimen originated from a patient with clinical symptoms and signs consistent with pneumonia, and new, persistent, or worsening pulmonary exudates, infiltrates, or consolidations are observed on imaging. Patients receiving antimicrobial treatment

who initially improved but then worsened, with a timing consistent with the appearance of pathogens, were included. Sputum cultures showing pathogen growth or predominant growth on two or more occasions were included. Moreover, biomarkers such as C-reactive protein and procalcitonin were beneficial supplements for clinical diagnosis.

Data Collection

The following data were retrospectively collected: patient data, including (1) demographic information, on sex and age; (2) underlying diseases, such as smoking history, alcohol history, diabetes, hypertension, chronic obstructive pulmonary disease, coronary heart disease, and number of underlying diseases; (3) admission status, such as transfer from another hospital, multiple injuries, chest trauma, coma, temperature, heart rate, and Glasgow Coma Scale (GCS); (4) early hospitalization laboratory results, such as creatinine clearance rate(CCR), albumin, hemoglobin, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR); (5) medication status, such as the combination of antibacterial drugs, days of antibacterial drug use, proton pump inhibitors, and glucocorticoids; and (6) other data, such as external ventricular drainage, surgical history, blood transfusion, urinary catheter, gastric tube, tracheostomy, mechanical ventilation time, and days of hospitalization before infection. This study was approved by the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (Ethics No. 2024-RE-444). As the study was retrospective in nature and did not involve any interventions in patient diagnosis or treatment, the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China waived the requirement for obtaining informed consent from the patients. The study was conducted in compliance with the Declaration of Helsinki and adhered to the principles of medical ethics. The authors ensured the strict confidentiality of all patient information.

Statistical Analysis

Patients were retrospectively randomized into a training group (70%) and a validation group (30%). Data from the training group were used to construct the nomogram, whereas data from the validation group were used for validation. These variables are presented as the means [standard deviations (SDs)] or medians [interquartile ranges (IQRs)], and comparisons between the two independent groups were made via independent sample *t*-test or Mann–Whitney *U*-test. Categorical variables are expressed as numbers (N%), and intergroup differences were compared via chi-square tests or Fisher's exact tests. Stepwise regression analysis was used to screen significant parameters ($P<0.05$) from the univariate analysis. The identified independent factors were analyzed via a binary logistic regression model, with the results presented as odds ratios (ORs) and 95% confidence intervals (CIs). Finally, we performed the Hosmer–Lemeshow (HL) test on the results of the logistic regression model to assess calibration. The area under the receiver operating characteristic curve (AUC) was used to evaluate the model's discrimination ability. The optimal cutoff point and its sensitivity and specificity were determined via a receiver operating characteristic (ROC) curve based on the Youden index. Decision curve analysis (DCA) was employed to assess the clinical applicability of the nomogram. All tests were two-sided, and $p<0.05$ was considered statistically significant.

Results

Screening and Clinical Characteristics of the Research Participants

We retrospectively collected clinical data from 3397 patients. A total of 438 patients who met the criteria were included in the study (MDR pneumonia group: 208 patients; non-MDR pneumonia group: 230 patients). The incidence of MDR pneumonia in the neurosurgery ward reached 47.49%, with the top three being multidrug-resistant *Acinetobacter baumannii* (MDRBA) (46.15%), multidrug-resistant *Pseudomonas aeruginosa* (MDRPA) (18.75%), and multidrug-resistant *Klebsiella pneumoniae* (MDRKP) (16.83%). Table 1 lists the clinical characteristics and random grouping of the two groups. The 438 patients were randomly divided into a training group of 307 patients (MDR pneumonia group, N=150; non-MDR pneumonia group, N=157) and a validation group of 131 patients (MDR pneumonia group, N=58; non-MDR pneumonia group, N=73). The results revealed no statistically significant difference in the prevalence of MDR pneumonia between the two groups (P=0.379).

https://doi.org/10.2147/IDR.S527114

Table 1 Clinical Characteristics of the Patients in Training Group and Validation Group

	Training Group (n=307)					Validation Group (n=131)		P-value[a]
	MDR Pneumonia Group (n=150)	Non-MDR Pneumonia Group (n=157)	χ^2	Z	P-value	MDR Pneumonia Group (n=58)	Non-MDR Pneumonia Group (n=73)	0.379
Demographic information								
Sex (male)	108 (72%)	116 (73.9%)	0.138		0.710	43 (74.1%)	47 (64.4%)	0.356
Age (years)	58.00 (49.75–70.00)	62.00 (53.50–71.00)		−1.693	0.091	57.00 (49.50–67.00)	62.00 (53.50–74.00)	0.856
Underlying diseases								
Smoking history	13 (8.7%)	13 (8.3%)	0.015		0.903	5 (8.6%)	2 (2.8%)	0.256
Alcohol history	13 (8.7%)	15 (9.6%)	0.073		0.787	7 (12.1%)	3 (4.1%)	0.613
Diabetes	15 (10%)	25 (15.9%)	2.375		0.123	11 (19.0%)	8 (11%)	0.679
Hypertension	54 (36%)	70 (44.6%)	2.349		0.125	31 (53.4%)	30 (41.1%)	0.231
COPD	10 (6.7%)	13 (8.3%)	0.288		0.591	4 (6.9%)	3 (4.1%)	0.415
Coronary heart disease	9 (6.0%)	13 (8.3%)	0.600		0.439	4 (6.9%)	5 (6.8%)	0.912
Number of underlying diseases (≥2)	13 (8.7%)	18 (11.5%)	0.662		0.416	9 (15.5%)	9 (12.3%)	0.753
Admission status								
Transfer from other hospital	106 (70.7%)	107 (61.2%)	0.228		0.633	36 (62.1%)	38 (52.1%)	0.009
Multiple injuries	12 (8%)	12 (7.6%)	0.086		0.770	1 (1.7%)	4 (5.5%)	0.123
Chest trauma	26 (17.3%)	25 (15.9%)	0.110		0.740	7 (12.1%)	15 (20.5%)	0.835
Coma	61 (40.7%)	64 (40.8%)	0.000		0.986	25 (43.1%)	36 (49.3%)	0.257
Temperature	36.80 (36.50–37.03)	36.80 (36.50–37.20)		−1.706	0.078	37.00 (36.80–37.33)	36.90 (36.50–37.00)	0.078
Heart rate	86.50 (73.50–130.00)	86.00 (74.00–100.00)		−0.321	0.728	78.00 (69.50–98.25)	86.00 (77.00–102.00)	0.820
GCS	7.00 (5.00–10.00)	8.00 (6.00–11.00)		−1.828	0.068	7.00 (5.00–12.00)	7.00 (5.00–11.00)	0.589
Early hospitalization laboratory results								
CCR≥130 (mL/min/1.73 m^2)	73 (48.7%)	39 (24.8%)	18.792		**<0.001**	25 (43.1%)	14 (19.2%)	0.176
Albumin≤30 (g/L)	63 (42%)	31 (19.7%)	17.884		**<0.001**	24 (41.4%)	17 (23.3%)	0.888
Hemoglobin	86.50 (77.00–106.00)	111.00 (93.00–128.00)		−6.879	**<0.001**	89.00 (72.75–112.25)	121.00 (101.50–135.50)	0.052
Day 1 NLR	6.53 (3.16–12.49)	9.36 (5.59–15.27)		−3.401	**<0.001**	8.05 (5.23–11.61)	10.08 (5.38–17.06)	0.618

Day 1 PLR	171.19 (87.79–260.36)	180.22 (117.38–278.50)		−2.116	**0.034**	150.52 (115.22–212.49)	159.23 (117.87–254.49)	0.458
Day 3 NLR	8.99 (5.81–12.58)	11.69 (6.30–15.36)		−2.610	**0.009**	8.62 (5.84–9.80)	10.09 (6.91–13.41)	0.278
Day 3 PLR	197.14 (129.38–246.8)	212.90 (133.29–263.45)		−1.155	0.248	192.23 (119.42–224.98)	171.95 (126.38–226.13)	0.020
Medication status								
Combination of antibacterial drugs	55 (36.7%)	18 (11.5%)	26.881		**<0.001**	22 (37.9%)	10 (13.7%)	0.884
Days of antibacterial drug use (days)	8.00 (4.00–12.25)	5.00 (3.00–7.00)		−4.996	**<0.001**	6.00 (3.75–11.25)	5.00 (3.00–8.00)	0.210
Proton pump inhibitors	63 (42%)	60 (38.2%)	0.457		0.459	13 (22.4%)	22 (30.1%)	0.008
Glucocorticoids	96 (64%)	93 (59.2%)	0.736		0.391	33 (56.9%)	30 (41.1%)	0.009
Others								
External ventricular drainage	23 (15.3%)	22 (14.0%)	0.107		0.744	9 (15.5%)	7 (9.6%)	0.499
Surgical history	90 (60%)	93 (59.2%)	0.512		0.474	25 (43.1%)	40 (54.8%)	0.053
Blood transfusion	49 (32.7%)	31 (19.7%)	6.647		**0.010**	16 (27.6%)	16 (21.9%)	0.720
Urinary catheter	136 (90.7%)	144 (91.1%)	0.106		0.745	53 (91.4%)	66 (90.4%)	0.902
Gastric tube	133 (88.7%)	142 (90.4%)	0.259		0.611	52 (89.7%)	64 (87.7%)	0.751
Tracheotomy	129 (86%)	107 (68.2%)	13.743		**<0.001**	46 (79.3%)	50 (68.5%)	0.422
Mechanical ventilation time (days)	4.00 (0.00–8.00)	2.00 (0.00–5.00)	−3.120		**0.002**	3.00 (0.00–6.00)	2.00 (0.00–5.00)	0.274
Days of hospitalization before infection (days)	11.00 (6.00–15.25)	7.00 (5.00–10.00)		−4.622	**<0.001**	7.50 (5.00–13.00)	7.00 (5.00–10.00)	0.088

Notes: Data are shown as number (N%), mean ± standard deviation, or median (quartile). The p-value column is marked in bold with the 12 significantly different variables in the univariate analysis. [a]P-value for the comparison of each parameter in the two groups.

Abbreviations: COPD, chronic obstructive pulmonary disease; GCS, Glasgow Coma Scale; CCR, creatinine clearance rate; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

https://doi.org/10.2147/IDR.S527114

Risk Factors for Screening MDR Pneumonia

Table 1 shows the univariate analysis results, which identified 12 variables with significant differences in the training group: CCR≥130 mL/min/1.73 m^2, albumin≤30 g/L, hemoglobin, the Day 1 NLR, the Day 1 PLR, the Day 3 NLR, the combination of antibacterial drugs, the days of antibacterial drug use, blood transfusion, tracheostomy, mechanical ventilation time and the days of hospitalization before infection (P<0.05). We performed a stepwise regression analysis on the above 12 variables, excluding those with poor predictive performance or multicollinearity, and identified 6 predictive factors. We subsequently included these factors in a multivariate logistic regression analysis (Table 2), and the results revealed that CCR≥130 mL/min/1.73 m^2 (OR=2.87; 95% CI=1.603–5.319), lower Day 1 NLR (OR=0.956; 95% CI=0.927–0.985), albumin≤30 g/L (OR=2.568; 95% CI=1.347–4.896), lower hemoglobin (OR=0.972; 95% CI=0.96–0.985), the combination of antibacterial drugs (OR=3.68; 95% CI=1.877–7.216), and tracheostomy (OR=2.292; 95% CI=1.162–4.521) were independent risk factors for the occurrence of MDR pneumonia in neurosurgery ward patients.

Construction, Validation, and Evaluation of the Nomogram

We constructed a nomogram based on a multivariable logistic regression model, as shown in Figure 1. For the values of each predictor in the nomogram, a vertical line is drawn upward from each point, and the values of different variables correspond to different scores on the reference line at the top (scores ranging from 0 to 100). The scores corresponding to each predictor are summed to obtain a total score, and then a vertical line is drawn downward from the total score line to the probability line at the bottom to determine the probability of MDR pneumonia.

The AUCs for the nomogram in the training group and validation group were 0.816 (95% CI: 0.760–0.862) and 0.797 (95% CI: 0.720–0.874), as shown in Figure 2A and B. In the training group, the optimal cutoff value for the nomogram was 0.430, with a sensitivity of 0.656 and specificity of 0.807. In the validation group, the optimal cutoff value for the nomogram was 0.438, with a sensitivity of 0.740 and specificity of 0.759.

The calibration curves of the training group and the validation group were relatively consistent with the 45 - degree diagonal line, as shown in Figure 2C and D. The HL test results were not significantly different, indicating that the fit of the nomogram was satisfactory.

If the threshold probability is between 0.1 and 0.9 (which applies to any cohort), the clinical interventions guided by the nomogram will have greater net benefits, as shown in Figure 2E and F.

Discussion

For patients in the neurosurgery ward, when the central nervous system is damaged, acute immune responses can lead to secondary brain tissue injury, followed by activation of the sympathetic nervous system, which can cause immune suppression.[12] This immune suppression increases the incidence of MDR pneumonia. The inflammatory state triggered by MDR pneumonia may provoke a bystander autoimmune response against central nervous system antigens, thereby forming a vicious cycle.[13] MDR pneumonia has multifaceted effects on patients in the neurosurgery ward. For these

Table 2 Results of the Stepwise Regression Analysis

Predictor	β	P-value	OR	95% CI	
CCR≥130 (mL/min/1.73 m^2)	1.054	<0.001	2.87	1.603	5.139
Day 1 NLR	−0.045	0.003	0.956	0.927	0.985
Albumin≤30 (g/L)	0.943	0.004	2.568	1.347	4.896
Hemoglobin	−0.028	<0.001	0.972	0.96	0.985
Combination of antibacterial drugs	1.303	<0.001	3.68	1.877	7.216
Tracheotomy	0.83	0.017	2.292	1.162	4.521

Abbreviations: CCR, creatinine clearance rate; NLR, neutrophil-to-lymphocyte ratio.

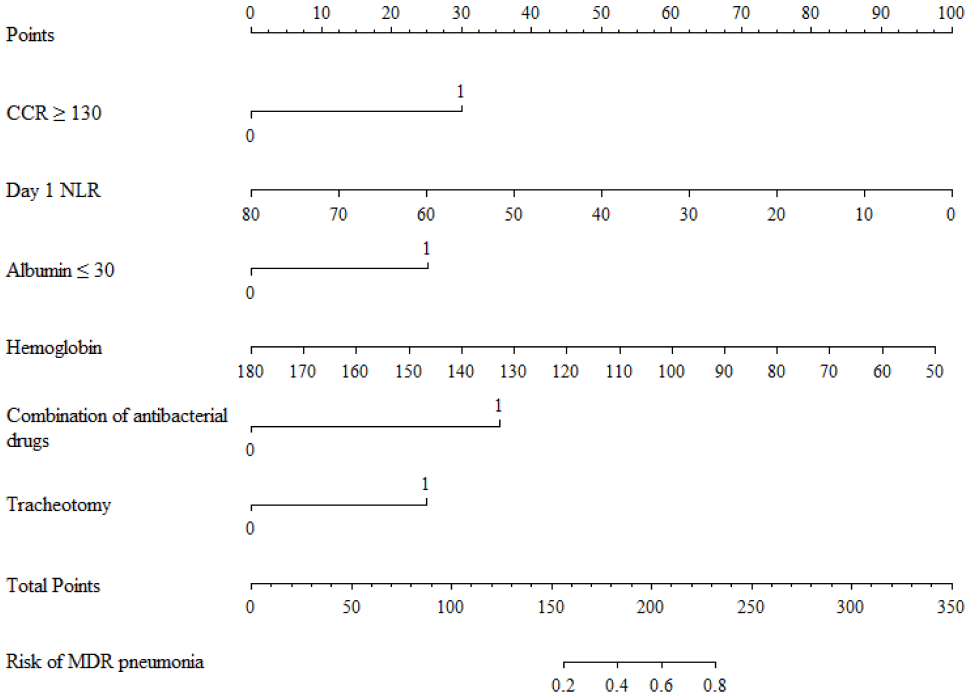

Figure 1 Example of prediction nomogram for the risk of multidrug-resistant (MDR) pneumonia.
Abbreviations: CCR, creatinine clearance rate; NLR, neutrophil-to-lymphocyte ratio.

patients, infection with MDR pneumonia not only prolongs hospital stays and increases mortality rates but also imposes a heavy economic burden. Therefore, identifying the patients who are at greater risk of developing MDR pneumonia is crucial.

Our study is based on clinical data from neurosurgery ward patients and uses effective mathematical modeling methods to analyze the data. The results indicate that CCR≥130 mL/min/1.73 m^2, a lower Day 1 NLR, albumin≤30 g/L, lower hemoglobin, combination of antibacterial drugs, and tracheostomy are independent risk factors for MDR pneumonia in neurosurgery ward patients. We subsequently developed a prediction nomogram consisting of these six predictive factors that has high sensitivity and specificity for the early identification of infection (training group AUC=0.816, validation group AUC=0.797). DCA revealed that this nomogram has significant potential for clinical application.

The incidence of MDR pneumonia among patients with pneumonia secondary to central nervous system injuries ranges from 8.5% to 42.2%.[1] This finding is generally consistent with our findings. In our study, a total of 438 patients with pulmonary infections were included, with an MDR infection rate of 47.49%. Gram-negative bacteria accounted for 86.06% of these infections, with MDRAB (46.15%), MDRPA (18.75%), and MDRKP (16.83%) being the most prevalent pathogens. This study detected only 21 strains (10.10%) of methicillin-resistant Staphylococcus aureus (MRSA), which is not surprising. According to data from the China Antimicrobial Surveillance Network (CHINET) from 2023, the prevalence of MRSA significantly decreased from 69.0% in 2005 to 29.6% in 2023.[14]

In recent years, the concept of augmented renal clearance (ARC) has been widely mentioned. It is characterized by an increase in CCR and an increase in the renal clearance of drugs.[15] In the intensive care unit (ICU), the incidence of ARC ranges from 33% to 65%.[16] Up to now, ARC has been defined as CCR of ≥130 mL/min/1.73 m^2.[17] In our study, we identified that a CCR of ≥130 mL/min/1.73 m^2, defining ARC, serves as an independent risk factor for MDR pneumonia among patients in the neurosurgical ward. To our knowledge, ARC has not previously been reported as a factor that influences risk. ARC primarily affects antimicrobial agents that are excreted by the kidneys, such as vancomycin, meropenem, ciprofloxacin, levofloxacin, and daptomycin, all of which are commonly used antimicrobial agents in the neurosurgical ward.[18] ARC leads to increased drug clearance, which can shorten the drug's half-life, reduce peak

https://doi.org/10.2147/IDR.S527114

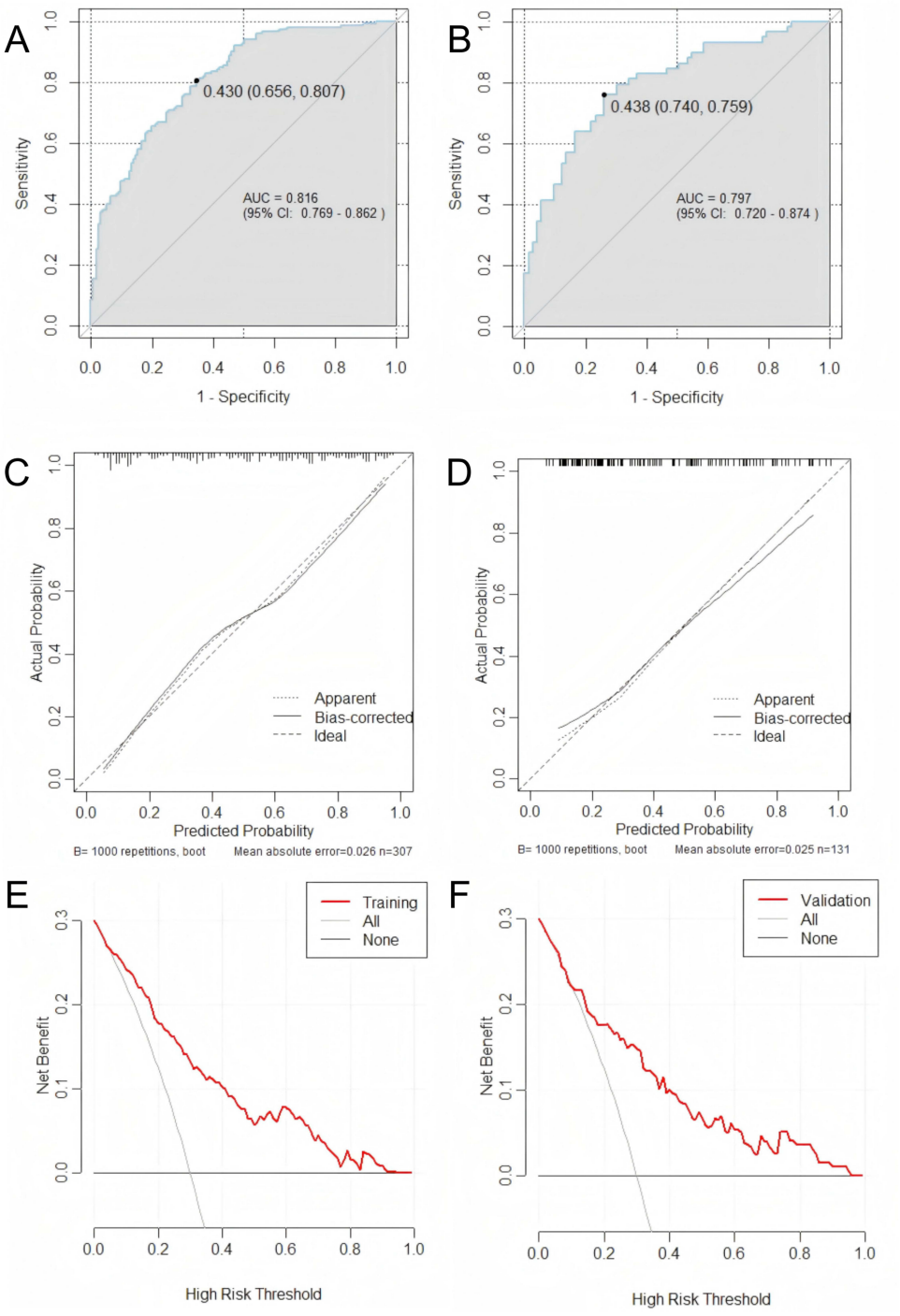

Figure 2 ROC curves, calibration curves, and DCA curves of the predictive nomogram in training group (**A, C** and **E**) and validation group (**B, D** and **F**).

concentrations, and decrease the area under the curve, changes that are likely to result in insufficient therapeutic drug concentrations. Studies have shown that, after administering the same dose of meropenem, the peak and trough concentrations of meropenem in ARC patients are only approximately half those in non-ARC patients.[19] Although most sensitive strains may continue to be killed when antimicrobial drug concentrations are insufficient, the pathogens cannot be completely cleared or suppressed, and the residual strains may proliferate significantly, potentially leading to resistance. Therefore, in view of the possibility of insufficient therapeutic drug concentrations, antimicrobial resistance, and even treatment failure caused by ARC, it is necessary to identify and diagnose ARC early. Measures such as

increasing the dosage, shortening the dosing interval, and continuous infusion should be adopted to compensate for the high clearance of antimicrobial drugs by the kidneys as much as possible, so as to reduce the occurrence of MDR pneumonia.

The NLR consists of two elements: neutrophils, which represent the nonspecific immune response, and lymphocytes, which embody adaptive cellular immunity, and their ratio becomes an indicator of the comparison between these two immune forces. Therefore, the NLR plays an important role in the inflammatory response process and can serve as a biomarker for immune responses triggered by various infectious and noninfectious stimuli.[20] Clinical studies have confirmed that the NLR has high sensitivity for the diagnosis and stratification of systemic infections, sepsis, and bacteremia, and it also has strong predictive value for disease prognosis.[21–23] Currently, most studies suggest that a higher the NLR corresponds to more severe the disease and a worse prognosis of patients.[21–24] Only a few studies have asserted the opposite. For example, a prospective study compared the mortality rates of patients with septic shock in the early (within 5 days of the onset of infectious shock) and late (after 5 days of the onset of infectious shock) stages and reported that patients who died early had a remarkable decrease in the NLR.[25] Additionally, Wu et al reported that a lower NLR was an independent risk factor for MDRBA pneumonia in patients with brain injury.[26] However, the mechanism remained unexplained. In our study, we simultaneously incorporated the NLR within the first three days of admission and found that only the Day 1 NLR was an independent risk factor for MDR pneumonia. Given that our findings were consistent with those of Di Wu et al, we hypothesize that this result may be related to our study population. The complex immunological dysregulation mechanisms in neurosurgical patients may contribute to the increased risk of MDR pneumonia. This could involve trauma-induced production of high levels of stress hormones (eg, adrenaline), which in turn increase lymphocyte counts and lead to a lower NLR.[27] Therefore, when interpreting the predictive value of Day 1 NLR, its clinical applicability may be limited to neurosurgical patients with MDR pneumonia. Further research is needed to elucidate the exact underlying mechanisms of inflammatory imbalance in this specific population.

Our research indicates that albumin≤30 g/L is a risk factor for patients in neurosurgery wards to develop MDR pneumonia, which is consistent with the findings of Qin et al.[28] Additionally, other studies have also confirmed that patients with hypoproteinemia are 2.07 times more likely to be infected with MDR strains than patients with normal albumin levels.[29] The development of MDR pneumonia in patients with hypoproteinemia is a complex process. First, hypoproteinemia directly leads to a decrease in plasma albumin levels, which in turn affects the synthesis of immunoglobulins and the activation of complement, increasing the vulnerability of the patient's immune system to external pathogens.[30] Moreover, hypoproteinemia also impacts the production and function of cytokines, weakening immune response capabilities.[31] Furthermore, current scholars have proposed that human serum albumin can alter the expression of specific genes, which promotes the survival and persistence of AB.[32] Although the phenomenon of hypoproteinemia leading to MDR pneumonia is widely recognized, the impact of hypoproteinemia on the pharmacokinetics of antimicrobial drugs is often overlooked when analyzing its causes. A decrease in plasma albumin in patients leads to an increase in the free drug concentration, which is rapidly distributed to the extravascular space, resulting in a decrease in drug concentration. The increased free drug concentration also increases drug clearance rate, which further reduces the drug concentration.[33] This situation is particularly pronounced with antimicrobial drugs that have a high protein binding rate, such as ceftriaxone, cefoperazone, and vancomycin, which are commonly used in neurosurgery wards. Therefore, the decrease in antimicrobial drug concentration and insufficient initial doses of antimicrobial drugs are also reasons for hypoproteinemia leading to MDR pneumonia. Notably, a decrease in hemoglobin levels usually also indicates that a patient's nutritional status is compromised and that immune function is weakened, thereby increasing susceptibility to infection.

In the neurosurgery ward, the combination of antimicrobial drugs is quite common and is aimed at broadening the antimicrobial spectrum, enhancing antimicrobial effects, and preventing the development of resistance. However, when deciding whether to combine antimicrobial drugs, we need to exercise caution, and the combination regimen should be based more on high-quality evidence from evidence-based medicine. For example, a study revealed that in the treatment of pneumonia caused by MRSA and MDRPA, combination therapy did not significantly differ from monotherapy in terms of cure rates and instead increased the resistance of pathogens.[34] In the treatment of adult MDRBA, among various combination regimens, only the combination of colistin and sulbactam demonstrated a relatively high bacterial clearance

rate and a relatively low incidence of adverse reactions.[35] Combination therapy also involves timely de-escalation. For critically ill neurological patients, the use of initial empirical combination therapy or broad-spectrum antimicrobials is feasible, but after microbiological and susceptibility results are obtained, the treatment regimen should be immediately reassessed, with a reduction in the number of antimicrobial agents or a decrease in the level of antimicrobial drugs. However, although timely de-escalation based on microbiological and susceptibility results has been proven safe for critically ill patients, more than 50% of antimicrobial treatments fail to achieve timely de-escalation.[36] Inappropriate combination therapy and failure to de-escalate in a timely manner will undoubtedly accelerate the emergence of resistant bacteria, and our research has confirmed this effect.

Most neurosurgical patients have respiratory dysfunction, and to ensure airway patency, tracheostomy is often required to maintain effective breathing. Tracheostomy is an invasive procedure that directly exposes the airway mucosa to the air, resulting in the loss of the body's natural defense functions, such as filtration and humidification.[37] This exposure allows many bacteria to invade the airway, thereby increasing the risk of lung infections. As the duration of mechanical ventilation after tracheostomy increases, the probability of cross-infection in patients also increases, which can easily lead to the proliferation and long-term colonization of respiratory pathogens, subsequently inducing the production of resistance genes.[38] Studies have shown that patients with a history of tracheostomy have a greater risk of developing MDR pneumonia.[39] Our research also confirmed this situation; among the surveyed patients, those who underwent tracheostomy had an incidence of MDR pneumonia that was 2.29 times greater than that of patients who did not undergo tracheostomy.

This study has the following advantages: First, we propose for the first time that ARC is an independent risk factor for the occurrence of MDR pneumonia in neurosurgical patients, and we provide a reasonable explanation for this finding. Given the high incidence of ACR in neurosurgical wards, this topic should receive significant attention from clinicians. Second, this research provides a convenient and practical quantitative prediction tool that is based on six predictive factors, which are all essential clinical indicators. These indicators are easy to test and cost effective and do not impose additional medical expenses on patients during hospitalization. Finally, our nomogram has been extensively validated, demonstrating good discrimination, calibration, and strong clinical applicability and stability.

However, this study also has certain limitations: It is a retrospective record of patient information from a single center over nearly four years and did not use external data for validation. Therefore, its generalizability to other populations may be limited. In the future, it will be necessary to incorporate multi-center, large-sample external datasets to more comprehensively evaluate the robustness of the model.

Overall, our nomogram includes six predictive factors: ARC, the Day 1 NLR, hypoproteinemia, hemoglobin, the combination of antibacterial drugs, and tracheostomy, which can predict the occurrence of MDR pneumonia in neurosurgical patients early during hospitalization. Based on the predictive results, adjustments can be made to the antimicrobial drug administration regimen, nutritional support, and clinical care. Moreover, early pulmonary pathogen testing can be conducted to accelerate the transition from empirical treatment to targeted therapy, thereby improving patient management. However, whether patients in the neurosurgery ward can benefit from the prevention and treatment of MDR pneumonia under the guidance of the nomogram still needs to be verified through prospective cohort studies, and we plan to conduct follow-up prospective research in the future.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author (duanwen1717@gmail.com) upon reasonable request.

Ethics Approval Statement

This study was approved by the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (Ethics No. 2024-RE-444). The study was conducted in compliance with the Declaration of Helsinki and adhered to the principles of medical ethics. The authors ensured the strict confidentiality of all patient information.

Funding

No funding was received for this study.

Disclosure

The authors report no conflicts of interest in this work.

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