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ARTICLE

Analysis of Risk Factors for Multidrug-Resistant Organism (MDRO) Infections and Construction of a Risk Prediction Model in a Cancer Specialty Hospital

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Abstract

Aims/Background Patients receiving treatment in specialized cancer hospitals are particularly susceptible to multidrug-resistant organisms (MDRO) infections due to factors such as weakened immune systems caused by intensive treatments and prolonged hospital stays. This study aims to investigate the risk factors for MDRO infections in the cancer specialty hospital setting and to develop a corresponding risk prediction model.

Methods Patients diagnosed with MDRO infections were selected for the MDRO infection group (n = 238), and those without for the non-MDRO infection group (n = 238). Non-parametric tests, chi-square tests, and multivariate logistic regression analysis were used to identify the primary risk factors for MDRO infections. With the aid of analysis utilizing R software 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria), we developed a nomogram prediction model, which was evaluated using the receiver operating characteristics (ROC) curve, calibration curve, and decision curve analysis (DCA).

Results Age, antibiotic application time, and central venous catheterization were independent risk factors for MDRO infection ($p < 0.05$). The constructed nomogram prediction model for patients with MDRO infection has a C-index of 0.8640. The ROC curve results showed that the prediction model has a specificity of 0.7700, a sensitivity of 0.8800, and an area under the curve (AUC) of 0.8800.

Conclusion This study identifies significant risk factors for MDRO infections in a cancer specialty hospital setting and offers a clinically useful prediction model, which may aid in targeted preventive measures and optimization of antibiotics usage, thereby potentially reducing the incidence and impact of these infections.

Key words: cancer specialty hospital; multidrug-resistant organisms; risk factors; prediction model; nomogram

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Introduction

In recent years, the widespread use of broad-spectrum antibiotics has precipitated a significant increase of multidrug-resistant organisms (MDRO) infection rate, accompanied by rapidly evolving bacterial resistance (Parmanik et al, 2022). Data indicated that approximately 2 million nosocomial infections occur annually in the United States, resulting in 60,000 to 90,000 deaths (Oliva et al, 2018). In China, the prevalence of hospital-acquired infections ranges between 6% and 8% (Oliva et al, 2018). It is worthy to note that infections caused by MDRO not only extend the treatment duration for patients but also elevate mortality rates (Dunn et al, 2019; Sarda et al, 2019). Given these dire consequences attributed to MDRO infections, it is essential to identify potential infection risk factors and implement timely interventions as part of the infection control efforts (Liu et al, 2023; Mills and Marchaim, 2021).

Cancer patients represent a high-risk group for MDRO infections. According to research reports, the MDRO infection rate in cancer patients is about 8.1% to 39.7% (Stratmann et al, 2020; Park et al, 2024), a rather wide range that indicates the impact of cancer type and treatments employed. Patients with cancer suffer from compromised physical functions and a high incidence of underlying diseases, requiring treatments such as surgeries, radiotherapy, chemotherapy, steroids and antibiotics, and catheterization, which especially anticancer treatments may elicit complications such as hypoproteinemia and bone marrow suppression after admission (Nanayakkara et al, 2021; Patel et al, 2021). These factors diminish the patient's innate infection resistance and increase the risk of infections. Thus, analyzing the high-risk factors for MDRO infections in the cancer specialty hospital setting would provide insights regarding prevention, control, and empirical antibiotic treatment of MDRO infections, while enhancing clinical practitioners' awareness of MDRO. However, existing research on this topic mainly focuses on settings in intensive care units (ICU) and burn units (De Waele et al, 2020; Hashemzadeh et al, 2022), with few studies exploring the risk factors for MDRO infection in cancer specialty hospitals.

Nomogram is a quantitative statistical tool initially adopted by the Memorial Sloan Kettering Cancer Center for the prognosis prediction of gastric cancer, which has then broadened its application since in the prediction of pathogenic infection risks across various patient groups (Ma et al, 2021; Yan et al, 2022). Identification of independent risk factors for MDRO infections through logistic regression analysis is the prevailing research trend, as evidenced by most studies, which did not attempt to employ nomograms for a visual and practical representation of the identified risk factors. Therefore, in this study, we investigated the risk factors for MDRO infections in a cancer specialty hospital and further constructed a nomogram prediction model, aiming to provide clinical references for improving the prognosis of hospitalized cancer patients.

Methods

Study Participants

A retrospective analysis was conducted on 476 patients who were treated at the Nantong Tumour Hospital, Nantong, China from November 2019 to January 2023. Patients who were diagnosed with MDRO infections through drug sensitivity tests and resistant organism monitoring were selected for the MDRO infection group (n = 238), and those without MDRO infections were chosen for the non-MDRO infection group (n = 238). Balanced sample sizes (i.e., equal number of subjects recruited) in both groups were employed to improve the statistical power and reliability of the analysis and help reduce bias attributed to sample imbalance. The study was approved by the Ethics Committee of Nantong Tumour Hospital (No. 2020-034). All procedures in this human study were performed in accordance with the Declaration of Helsinki (as revised in 2013), and all patients signed informed consent.

The inclusion criteria of this study are as follows: (1) patients who had no bacterial infections prior to hospital admission; (2) patients who had been hospitalized for >48 hours; and (3) patients who had given informed consent to participate, with their complete medical records available. Individuals with the following exclusion criteria were excluded from the study: (1) patients with critical conditions; and (2) patients who did not provide informed consent or whose clinical data were incomplete.

Data Collection

A retrospective analysis was conducted, collecting baseline and clinical data from cancer patients whose samples were acquired by the microbiology department for pathogen isolation. The information gathered include: (1) basic patient information such as gender, age, underlying diseases, etc.; (2) antibiotic usage; and (3) situations involving invasive procedures, such as central venous catheterization, tracheal intubation/tracheostomy, gastric tube, urinary catheterization, etc.

Statistical Analysis

This study utilized SPSS 26.0 (IBM Corp., Armonk, NY, USA) for data analysis. Shapiro–Wilk test was utilized to assess the data conformance to normal distribution. Quantitative data for variables like age and antibiotic application time, which are not normally distributed, are expressed as median (P_{25}, P_{75}) and were analyzed using Mann-Whitney tests to identify univariate factors significantly associated with MDRO infection. Categorical data are presented as count and were analyzed using a chi-square (χ^2) test to identify significant univariate factors. A multivariate logistic regression model was used for multivariate analysis to identify independent risk factors for MDRO infection in hospitalized patients. Nomogram prediction models for MDRO infection, receiver operating characteristics (ROC) curve, calibration curve and decision curve analysis (DCA) were constructed using the rms package in R software 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria). A p-value < 0.05 was considered statistically significant.

Results

Univariate Analysis of Baseline and Clinical Data

The chi-square test revealed that age, prolonged bed rest, history of diabetes, number of antibiotics used concurrently, antibiotic application time and chemotherapy were significantly associated with MDRO infection ($p < 0.05$). The age and antibiotic application time in the infected group were significantly higher than those in the non-infected group ($p < 0.05$). Additionally, in the MDRO infection group, the proportions of patients with prolonged bed rest, using more than one type of antibiotic, having diabetes, and undergoing chemotherapy were significantly higher ($p < 0.05$) (Table 1).

Univariate Analysis of Invasive Procedures

The chi-square test uncovered that tracheal intubation/tracheostomy, central venous catheterization, and urinary catheter retention were significantly associated with MDRO infection ($p < 0.05$). The proportions of patients in the infected group who underwent tracheal intubation/tracheostomy, central venous catheterization, and urinary catheter retention were significantly higher ($p < 0.05$) (Table 2).

Multivariate Logistic Regression Analysis

Based on the outputs from multivariate logistic regression analysis, age, antibiotic application time and central venous catheterization were independent risk factors for MDRO infection ($p < 0.05$) (Table 3).

Nomogram Prediction Model

Based on the results of the multivariate binary logistic regression analysis, a nomogram prediction model for estimating the risk of MDRO infection in hospitalized cancer patients was constructed using the rms package in R language, incorporating age, antibiotic application time, and central venous indwelling catheterization as predictive factors (Fig. 1A). This model can be used to help compute the score for each independent risk factor based on the patient's actual condition. By summing the scores of each factor, the total score of each patient can be calculated. This total score corresponds to a value on the "Total Points" scale, which can then be matched to a reading on the "RISK" axis to determine the patient's risk of MDRO infection.

In this study, the C-index of the model was 0.8640 (95% confidence interval (CI): 0.8312–0.8987). The Hosmer–Lemeshow goodness-of-fit test indicated that there was no significant difference between the estimated probability of MDRO infection in hospitalized patients and the actual infection rate ($\chi^2 = 14.27$, $p = 0.0749$), suggesting good predictive performance of the model. Additionally, the calibration curve is closely aligned with the ideal curve (Fig. 1B). Within the high-risk threshold range of 0.16 to 1.00, the model can accurately predict the occurrence of MDRO infection among the tested patients (Fig. 1C). The ROC curve results showed an area under the curve (AUC) of 0.8800 (95% CI: 0.8400–0.9200), a specificity of 0.7700 (95% CI: 0.7000–0.8300), and a sensitivity of 0.8800 (95% CI: 0.8300–0.9300) (Fig. 1D).

Table 1. Univariate analysis of baseline and clinical data.

Factors	MDRO infection group (n = 238)	Non-MDRO infection group (n = 238)	Z/χ^2	*p*-value
Age	68.00 (58.00, 75.00)	50.00 (44.00, 56.00)	–13.15	<0.0001
Gender			0.3261	0.5680
Male	154	148		
Female	84	90		
Prolonged bed rest			20.87	<0.0001
Yes	49	15		
No	189	223		
History of hypertension			0.1741	0.6765
Yes	31	28		
No	207	210		
History of diabetes			7.195	0.0073
Yes	38	19		
No	200	219		
History of coronary heart disease			0.4934	0.4824
Yes	8	11		
No	230	227		
Number of antibiotics used concurrently			5.301	0.0214
≤1	142	166		
>1	96	72		
Antibiotic application time (days)	5.00 (4.00, 7.00)	4.00 (3.00, 6.00)	–6.103	<0.0001
Radiotherapy			0.0408	0.8399
Yes	68	70		
No	170	168		
Chemotherapy			4.228	0.0398
Yes	199	181		
No	39	57		
Targeted therapy			0.0809	0.7760
Yes	87	90		
No	151	148		

Abbreviation: MDRO, multidrug-resistant organisms. Boldface *p*-values indicate statistical significance at $p < 0.05$.

Discussion

Risk factors for MDRO infections cover a range of both endogenous and exogenous factors. Endogenous factors pertain to a patient's inherent immune function and overall health condition. It is widely acknowledged that older patients, especially those confined to prolonged bed rest, experience a decline in physiological functions and immune capabilities, which reduces their resistance to pathogenic infections (Nohl et al, 2022). Patients with diabetes, characterized by elevated blood glucose levels, face increased plasma osmotic pressure and diminished phagocytic activity of white blood cells against pathogens, which pave the way for pathogenic invasion and infections (Magira et al, 2018). Chang et al (2022) identified that

Table 2. Univariate analysis of invasive procedures.

Factors		MDRO infection group (n = 238)	Non-MDRO infection group (n = 238)	χ^2	*p*-value
Tracheal intubation/tracheostomy	Yes	21	10	4.175	0.0410
	No	217	228		
Central venous catheterization	Yes	43	12	19.76	<0.0001
	No	195	226		
Indwelling gastric tube	Yes	25	29	0.3155	0.5743
	No	213	210		
Urinary catheter retention	Yes	39	12	16.01	<0.0001
	No	199	226		
Chest drainage	Yes	6	8	0.2944	0.5874
	No	232	230		

Abbreviation: MDRO, multidrug-resistant organisms. Boldface *p*-values indicate statistical significance at $p < 0.05$.

Table 3. Multivariate logistic regression analysis.

Influencing factors	β	SE	Wald	*p*	OR (95% CI)
Age	0.116	0.012	92.522	<0.0001	1.123 (1.097–1.150)
Antibiotic application time	0.231	0.064	12.873	0.0003	1.259 (1.110–1.428)
Prolonged bed rest	–0.112	0.469	0.058	0.8103	0.894 (0.357–2.239)
Chemotherapy	0.533	0.307	3.011	0.0827	1.704 (0.933–3.112)
History of diabetes	0.262	0.414	0.401	0.5268	1.300 (0.577–2.929)
Number of antibiotics used concurrently	0.484	0.258	3.531	0.0602	1.623 (0.979–2.689)
Tracheal intubation/tracheostomy	0.277	0.545	0.258	0.6112	1.319 (0.453–3.838)
Central venous catheterization	1.187	0.449	7.008	0.0081	3.278 (1.361–7.897)
Urinary catheter retention	0.419	0.448	0.873	0.3501	1.520 (0.632–3.656)

Abbreviations: SE, standard error; OR, odds ratio; CI, confidence interval. Boldface *p*-values indicate statistical significance at $p < 0.05$.

an age of ≥60 years, a history of diabetes, and prolonged bed rest are independent risk factors for MDRO infections in patients with malignant tumours. Exogenous factors include invasive procedures, the non-judicious use of antibiotics, and environmental conditions within the hospital. Procedures such as central venous catheterization, tracheal intubation, and prolonged urinary catheter retention disrupt normal physiological barriers and local immune function defenses, thereby increasing infection risks.

A study from Taiwan found a significantly higher prevalence of central venous catheter use in patients with multidrug-resistant bacteremia compared to those afflicted with the non-resistant variant of the condition (87.1% vs 73.2%) (Wattal et al, 2020). Similarly, Zhou et al (2020) highlighted that invasive procedures markedly increase the likelihood of MDRO infections among patients with malignant tumours, as these interventions can compromise the patient's immune. Pathogens tend to adhere to the surfaces of catheters, escalating the risk over time; how-

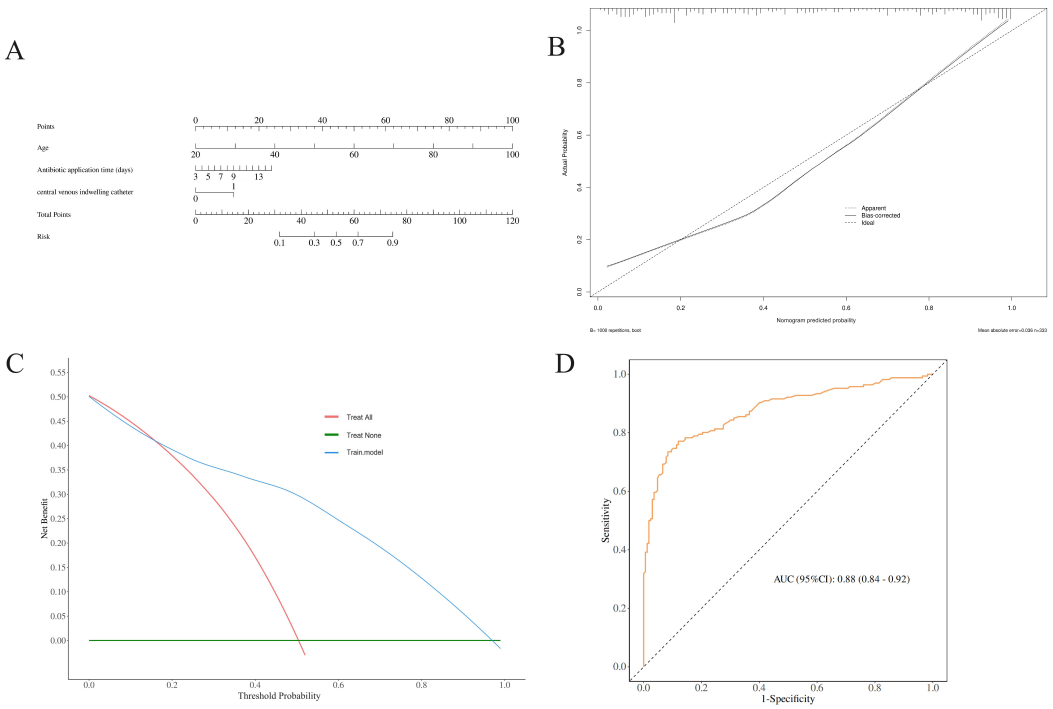

Fig. 1. The overall analysis results. (A) Nomogram prediction model was designed based on the data derived from patients admitted to a cancer specialty hospital. (B) Calibration curves. (C) Decision curve analysis (DCA) curve. (D) Receiver operating characteristics (ROC) curve. AUC, an area under the curve.

ever, frequent changes of catheters may also elevate the risks of infection. Further studies have shown that the antibiotic application time, the types of antibiotics used, and the use of more than three antibiotics are independent risk factors for MDRO infections (Campion and Scully, 2018; Nohl et al, 2022). Sun et al (2021) noted that antibiotic treatment exceeding 14 days significantly heightens the risk for MDRO infections in patients with malignant tumours. Consistent with these findings, our study demonstrates the significant links of MDRO infections with several risk factors, such as advanced age, prolonged bed rest, history of diabetes, the number of antibiotics used concurrently, antibiotic application time, tracheal intubation/tracheotomy, central venous catheterization, and urinary catheter retention. Notably, the subjects in the MDRO infection group had a higher average age and used antibiotics for a longer time compared with those in the non-MDRO infection group. Moreover, the proportion of patients in the infected group who experienced prolonged bed rest, utilized multiple antibiotics, or had diabetes was significantly higher than in the non-infected group. The number of patients in the infected group who underwent tracheal intubation/tracheotomy, central venous catheterization, and urinary catheter retention were also significantly higher.

Separately, multivariate logistic regression analysis showed that age, antibiotic application time, and central venous catheterization are independent risk factors for MDRO infections among hospitalized patients with cancer. The significant association between older age and higher susceptibility to MDRO infections serves as a potential indicator of the cumulative impact of comorbidities and the physiological

decline associated with ageing, including diminished immune response (Madrazo et al, 2021). The prolonged antibiotic usage, which is one of the independent risk factors for MDRO infections, is a probable cause of the disruption of normal microbial flora, favouring the growth of resistant organisms. This underscores the critical need for antibiotic stewardship programs that promote the judicious use of antibiotics, including regimen selection based on culture and sensitivity results, dose optimization, and shortening of treatment duration (Murray et al, 2019).

The strong association of invasive procedures like central venous catheterization with MDRO infections points to the disruption of natural barriers and the subsequent body invasion by external pathogens (Pitiriga et al, 2020). Our findings emphasize the need for stringent aseptic techniques, the judicious selection of catheter sites, and possibly the use of antimicrobial-coated catheters to reduce the risk of infections. Consequently, intensive monitoring of vital signs and meticulous management of antimicrobial therapies are imperative to mitigate infection risks in patients exhibiting these risk factors.

In recent years, nomograms have been widely applied in predicting the risk of nosocomial infections. Aside from making infection risks more visual, the nomogram demonstrated good predictive performance, which is conducive to clinical decision-making. Tang et al (2023) reported that their prediction model incorporating factors like carbapenem usage, antibiotic use for more than 7 days, tracheal intubation, nasogastric tube use, ICU stay of longer than 7 days, and ventilator usage had good discriminative power and reliability, which are attributes indicative of the model's clinical applicability. A nomogram prediction model developed by Wang et al (2020) for multidrug-resistant bacteria infection incorporating factors like gender, C-reactive protein level, and Pitt bacteremia score can help clinical staff estimate infection risk, providing a specific probability of infection.

Based on the results of the multivariate logistic regression analysis, we constructed a nomogram prediction model for MDRO infection using the R package 'rms'. The model's C-index of 0.8640, which exceeds 0.8, indicates good predictive performance. The Hosmer–Lemeshow goodness-of-fit test showed no significant difference between the predicted probabilities of MDRO infection and the actual probabilities in hospitalized patients, with the calibration curve approaching the ideal line. The decision curve indicated that using this prediction model can accurately predict the occurrence of MDRO infection among the tested patients at a high-risk threshold between 0.16 and 1.00. The ROC curve results also demonstrated that this model has good predictive performance, marked by high AUC, sensitivity, and specificity.

Conclusion

The current study recommends that antibiotic application duration and central venous catheterization are key independent risk factors for MDRO infections in patients receiving treatment in a cancer specialty hospital setting. By utilizing these factors, we developed a nomogram that effectively predicts the risk for MDRO infections, facilitating early identification of high-risk patients and enabling timely

preventive interventions. Insights from this study are crucial for healthcare professionals to devise targeted strategies that optimize antibiotic use and enhance infection control measures, ultimately reducing the incidence and impact of MDRO infections in hospitals.

Key Points

- The study investigates key risk factors for multidrug-resistant organism (MDRO) infections in patients treated at a cancer specialty hospital.
- Through comprehensive statistical analysis, the research identified age, antibiotic application duration, and central venous catheterization as significant independent risk factors for MDRO infections.
- Utilizing these findings, a nomogram-based risk prediction model was constructed and evaluated for its accuracy, with an area under the curve (AUC) of 0.8800, showing good predictive performance.
- The study concludes that the model can aid clinicians in identifying high-risk patients and tailoring preventive strategies, thereby optimizing antibiotic use and potentially reducing MDRO infections in this vulnerable patient population.

Availability of Data and Materials

All experimental data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

CL conceived and designed the study. JX and XC provided study materials or patients. LH and LW were responsible for the collection and assembly of data. JX, XC, HZ, PM, and YY conducted data analysis and interpretation. YY drafted the manuscript. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of Nantong Tumour Hospital (NO. 2020-034). All procedures in this human study were performed in accordance with the Declaration of Helsinki (as revised in 2013), and all patients signed informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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