

Clinical and microbiological characteristics of MRSA pneumonia in ICU patients and therapeutic effect of linezolid

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Abstract: The clinical and microbiological features of methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia among intensive care unit (ICU) patients were assessed in this study, as well as the relationship between linezolid treatment and outcomes. Of 282 ICU patients (January 2019-March 2024), 176 survived and 106 passed away. Independent predictors of death were age >60 years, tracheal intubation, central venous catheterization, ≥ 3 comorbidities and elevated procalcitonin (PCT). Seventy-two sputum representative MRSA isolates were analyzed for resistance determinants (*mecA*, *SCCmec*) and prevalent virulence genes (*sea*, *hla*, *tsst-1*, *icaA*, *pvl*). Linezolid therapy was associated with improved survival, reduced PCT levels and reduced prevalence of *sea*, *tsst-1* and *icaA*. *pvl* co-presence with other virulence genes was related to poor outcomes. Including use of linezolid in predictive models improved discrimination (ROC AUC 0.805). Transfusion recipients frequently present with independent risk factors associated with mortality in ICU patients diagnosed with MRSA pneumonia. Prognosis for ICU MRSA pneumonia is based on clinical risk factors, virulence gene carriage and transfusion status. Limitations are the retrospective study design and that sputum samples were used, which may result in misclassification.

Keywords: Clinical characteristics; ICU; Linezolid; MRSA pneumonia; Pvl; Virulence genes

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INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most common causes of hospital-acquired infection (HA-MRSA), transmitted primarily through the hands of healthcare professionals and contaminated medical devices (Pickens & Wunderink, 2022; Hyun *et al.*, 2022). Older patients and those who are immunocompromised are particularly susceptible, especially those who receive invasive procedures such as endotracheal intubation or central venous catheterization. MRSA is the most common Gram-positive antibiotic-resistant cause of hospital-acquired pneumonia, with resistance to macrolides, lincosamides and nearly all β -lactams and with occasional reduced vancomycin susceptibility (Guo *et al.*, 2020). MRSA infection has high morbidity and mortality and it is a serious challenge in intensive care unit (ICU) settings worldwide (Loaiza *et al.*, 2023; Solmaz *et al.*, 2021).

Critically ill MRSA pneumonia patients are particularly at risk based on the convergence of critical illness, bacterial virulence and multidrug resistance (Patel & Rawat, 2023). *Sea*, *tsst-1* and *icaA* virulence factors promote bacterial adhesion, biofilm formation and invasion of tissue, eliciting host inflammatory responses and leading to severe respiratory dysfunction (Silva *et al.*, 2021). Classic antibiotics like vancomycin are increasingly limited by diminished effectiveness or failure in therapy (Ibrahim *et al.*, 2023; Ismael *et al.*, 2023). However, most of the studies focus on antimicrobial resistance while the combined

effect of clinical factors and virulence gene patterns on patient outcomes remains to be thoroughly examined.

Linezolid, an oxazolidinone, is a protein synthesis inhibitor in bacteria that binds the 50S ribosomal subunit and has been a good choice for treating MRSA infections, even in decreased vancomycin susceptible strains. It has good penetration into alveolar lining fluid and lung tissue and also comes in intravenous and oral formulations, allowing flexible administration and early transition to oral therapy (Kawasuji *et al.*, 2023; Yayan *et al.*, 2015). Some studies have reported that linezolid use is associated with lower rates of major virulence genes (*sea*, *tsst-1*, *icaA*), yet these associations remain correlative to a significant degree (Pletz *et al.*, 2010; Dennis *et al.*, 2002). Clinical evidence also points towards linezolid improving survival, lowering inflammatory markers such as procalcitonin (PCT) and C-reactive protein (CRP) and lowering recovery time for ICU patients with severe pneumonia (AbdAlhafiz *et al.*, 2023; Gatti *et al.*, 2023; Papan *et al.*, 2021).

Because of the enhanced virulence, lethality and therapeutic challenge of ICU MRSA pneumonia, this study aimed: (1) to illustrate the clinical and microbiological presentation of MRSA pneumonia in ICU patients, (2) to determine the occurrence and frequency of key virulence genes and (3) to explore the association between linezolid treatment, outcome of the patient and virulence gene pattern. In addition, the study explored the value of prediction by adding linezolid use to outcome models to guide evidence-based, targeted interventions among high-risk ICU populations.

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MATERIALS AND METHODS

General material

282 MRSA pneumonia patients diagnosed retrospectively from January 2019 to March 2024 were recruited from Xuzhou Medical University Affiliated Hospital. They were 176 men and 106 women aged 62 ± 17 years. The patients were divided by outcome: survival ($n = 176$) and death ($n = 106$). The survival group was then subdivided into linezolid-treated ($n = 110$) and non-linezolid-treated ($n = 66$) groups. Survival was applied to describe resolution of symptoms and laboratory and imaging improvement, while non-cure described ongoing or worsening symptoms at discharge, transfer to higher care level, or in-hospital mortality.

Linezolid was initiated according to institutional ICU guidelines for suspected or confirmed MRSA pneumonia, based on clinical severity, e.g., elevated PCT, high SOFA score, or requirement for mechanical ventilation. Median time-to-first dose was 2 days (IQR 1-4) from receipt of cultures and median duration of treatment was 10 days (IQR 8-13). Comparator patients received standard anti-MRSA treatment (vancomycin or teicoplanin) based on patterns of susceptibility; vancomycin trough levels and MIC values were recorded where available. Sample of 282 patients was selected from all available cases of ICU MRSA pneumonia throughout the study duration; there was no formal power calculation due to the retrospective nature of the study and the sample was determined by the number of eligible cases identified in the ICU during the timeframe of the analysis.

Diagnostic criteria and patient selection

The diagnostic and selection criteria for the patient with pneumonia include community-acquired pneumonia (CAP), which is characterized by new onset of lower respiratory illness such as cough with purulent sputum, fever $>38^{\circ}\text{C}$ and abnormal white blood cell (WBC) count and chest imaging findings indicate patchy or interstitial infiltrates, with or without pleural effusion. Hospital-acquired pneumonia (HAP) is pneumonia that develops ≥ 48 hours from admission, with no preceding lower respiratory infection and new or worsening infiltrates and a minimum of two clinical findings, including fever $>38^{\circ}\text{C}$, abnormal WBC and purulent sputum. Study inclusion criteria were ICU patients with diagnostic criteria for pneumonia, with MRSA through sputum culture with oxacillin resistance ($\text{MIC} > 4 \mu\text{g/mL}$, ceftazidime method) and complete clinical records, with discharge or death outcomes that could be classified. Exclusion criteria included patients with indeterminate or mixed pneumonia in which MRSA was not the prevalent pathogen, ICU readmission within 30 days, death within the first 24 hours following ICU admission and patients who had received prior treatment with anti-MRSA antibiotics, although these were recorded but not included in the models for statistical adjustment.

Source of strain and sample collection

Sputum specimens were collected according to national clinical laboratory standards. In spontaneously expectorating patients, sputum was collected after oral rinsing; in non-expectorating patients, lower respiratory tract suction samples were collected. Specimens were processed within 2 hours. High-quality specimens contained <10 epithelial cells and >25 neutrophils per low-power field (ratio $<1:2.5$). Identification of MRSA employed broth microdilution with ceftazidime ($4 \mu\text{g/mL}$); $\text{MIC} > 4 \mu\text{g/mL}$ confirmed MRSA. A limitation of the study was the dependency on sputum samples, which may cause contamination or misclassification, particularly in non-expectorating patients.

Retrospective clinical data and statistical modelling

Patients were stratified by treatment (linezolid vs. non-linezolid) and outcome (survival vs. mortality). Univariate chi-square tests identified variables associated with mortality. Significant variables were entered into multivariate logistic regression to determine independent predictors of death. Multivariate model covariate selection was informed by clinical relevance. Variance inflation factors ($\text{VIF} < 2$) tested for multicollinearity. Missing values in key covariates were $<5\%$ and treated with complete-case analysis.

Virulence gene selection and isolate sampling

72 MRSA isolates from 282 cases were selected at random for molecular testing and 24 isolates from each of the three subgroups: treated survivors, untreated survivors and the death group. The isolates were selected to examine the presence of virulence genes and probe for any relationships with treatment outcomes. But it would be worth noting that this exploratory subgroup may not have sufficient statistical power for purposeful comparisons and the sample may well be a little unrepresentative of the entire cohort, limiting the ability to generalize the results to the wider population of patients.

Laboratory equipment and reagents

Routine laboratory gear used in the study included CO_2 incubators, -80°C freezers, biosafety cabinets, PCR thermocyclers and gel image systems required for generating controlled environments and performing accurate molecular assays. The reagents used included Columbia blood agar to isolate bacterial colonies, lysostaphin to extract DNA and PCR-grade reagents like primers, buffers and nucleotides used for resistance and virulence gene detection as well as SCCmec typing. These reagents and equipment played a crucial role in ensuring the accuracy and reliability of experiments conducted to investigate MRSA strains.

Strain enrichment

Frozen isolates of MRSA were revived by inoculating them on Columbia blood agar plates and further incubating at 35°C for 24 hours. Isolated colonies were individually selected and harvested post-incubation to yield a pure

culture. DNA was extracted from the colonies, thereby enabling subsequent molecular study as well as strain identification. Enrichment enables recovery of viable MRSA strains suitable for subsequent experiments such as PCR amplification and identification of virulence factors.

DNA extraction and PCR conditions

DNA was isolated by suspending 2-3 colonies in 300 µL of lysostaphin solution (30 U/mL in TE buffer, pH 8.0) and incubated at 35°C for 60 minutes and heat-treated at 100°C for 10 minutes. The lysates were centrifuged at 12,000 rpm for 5 minutes and the supernatants were stored at -80°C. The PCR cycle conditions were a first denaturation of 95°C for 5 minutes, followed by 35 denaturations of 95°C for 30 seconds, gene-specific annealing and extension at 72°C for 45 seconds. The final extension was at 72°C for 5 minutes. The PCR products were sequenced to confirm specificity. *mecC* and *mecA* were screened and SCCmec typing was carried out in accordance with established criteria with untyped isolates recorded.

MRSA validation, SCCmec typing and detection of virulence

MRSA validation was established via PCR amplification of *mecA*, *mecC*, as well as other virulence genes including *sea* (enterotoxin A), *hla* (alpha-hemolysin), *tsst-1* (toxic shock syndrome toxin-1), *icaA* (intercellular adhesion gene) and *pvl* (Panton-Valentine leukocidin) (Table 1). These genes are key markers to determine MRSA presence and its virulence capability. SCCmec typing was conducted to assign the right type, ranging from I to V, with subtypes IVa to IVd, which are of importance in MRSA stratification based on the architecture of its SCCmec element, which is a genetic cassette that hosts the *mecA* gene. In isolates which were non-typeable, the reading was recorded as not typed, which provided useful information regarding the genetic diversity of the MRSA isolates in the study population. Such a comprehensive approach allows for complete evaluation of antimicrobial resistance pattern and virulence factors, which are crucial for the understanding of the possible pathogenicity of MRSA within the health care setting.

Statistical analysis

Statistical analysis was done using SPSS v26.0. Continuous variables were presented as mean ± SD or median (IQR) and contrasted using t-test or Mann-Whitney U test, as appropriate. Categorical variables were presented as n (%) and contrasted using Chi-square or Fisher's exact test. Multiple gene comparisons were exploratory, with no Bonferroni adjustment. P value of <0.05 in a two-tailed test was considered statistically significant.

RESULTS

Univariate analysis of patient outcomes and mortality risk factors

282 patients in ICU with MRSA pneumonia were studied,

of whom 176 (62.4%) survived and 106 (37.6%) died. In the survivors, 110 patients received linezolid treatment. Patients treated with linezolid received earlier initiation (median 2 days, IQR 1-4 from collection of culture) and had a median treatment duration of 10 days (IQR 8-13). Univariate analysis identified age >60 years, tracheal intubation, central venous catheterization, diabetes, ≥3 comorbidities, low albumin and elevated inflammatory markers-procalcitonin (PCT), C-reactive protein (CRP), neutrophil percentage, lymphocyte count, PT and creatinine-as predictors for mortality (all $P < 0.05$ in tables 2 and 3). "Non-cure" was the result of prolonged infection or symptoms at discharge, transfer for further care, or death in hospital.

Multivariate logistic regression analysis

Multivariate logistic regression analysis identified several independent predictors of mortality in ICU MRSA pneumonia patients, including age >60 years, tracheal intubation, central venous catheterization, ≥3 comorbidities and high procalcitonin (PCT) levels. Notably, linezolid treatment was independently associated with a protective effect. These findings are detailed in Table 4, which shows the independent risk factors for death among ICU MRSA pneumonia patients. Fig. 1 illustrates the independent risk and protective factors for mortality, with the red dashed line indicating an odds ratio (OR) of 1. Risk factors associated with increased mortality are shown to the right of the line, while linezolid (OR <1) is depicted as a protective.

Predictive efficacy of risk factors

ROC analysis of independent risk factors showed AUC = 0.766 (95% CI 0.709-0.822, sensitivity 71.7%, specificity 68.2%, $P < 0.001$). Addition of linezolid therapy to predictive accuracy increased AUC to 0.805 (Fig. 2).

Transfusion and mortality risk factors

Transfused patients were more critically ill (higher PCT, more intubation). Linezolid use among transfused patients was associated with lower PCT and mortality.

Blood transfusion was excluded from logistic regression due to collinearity with PCT and intubation but exploratory Cox regression showed adjusted protective trends with linezolid (Table 5).

SCCmec genotyping, MRSA strain typing and virulence genes

Seventy-two MRSA isolates were randomly selected (24 for each outcome group) for molecular analysis, including the testing of resistance genes, SCCmec genotypes and virulence factors. This exploratory population does not have sufficient statistical strength for providing comprehensive subgroup analyses. Presence of the *mecA* gene with essential virulence genes within the above 72 MRSA isolates is summarized in table 6, providing insightful information concerning the distribution of pathogenic determinants across the isolates.

Table 1: PCR primer sequences and conditions

Gene	Primer sequence (5'→3')	Product size (bp)	Annealing temp (°C)
mecA	F: CAGAGTACAAAGGTTGGAAGG R: AAGGAGGATGATGAGTTGAGG	310	55
sea	F: ATGAAAGTAAAGGAAAGTGG R: TTAGAGGAGTAAAGGAGTGG	120	54
tsst-1	F: ATGAGTATTGAGTTGAGGAG R: TTAGAGGAGTAAAGGAGTGG	270	55
icaA	F: ATGGAAGTAAAGGAAAGTGG R: TTAGAGGAGTAAAGGAGTGG	131	56
hla	F: ATGACAAAGTTGTTGAGGAG R: TTAGAGGAGTAAAGGAGTGG	209	55
pvl	F: ATGACAAAGTTGTTGAGGAG R: TTAGAGGAGTAAAGGAGTGG	433	56

Table 2: Univariate analysis of demographic and clinical risk factors for ICU MRSA pneumonia mortality with, or without, linezolid treatment

Variable	Total (n=282)	Survival (n=176)	Death (n=106)	χ^2 / t / Z	P
Gender, F/M	106/176	59/117	47/59	$\chi^2=3.30$	0.069
>60 years, n (%)	185 (65.6)	106 (60.2)	79 (74.5)	$\chi^2=6.00$	0.014
Tracheal intubation, n (%)	216 (76.6)	119 (67.6)	97 (91.5)	$\chi^2=21.07$	<0.001
Central venous cannula, n (%)	197 (69.9)	113 (64.2)	84 (79.2)	$\chi^2=7.11$	0.008
≥3 comorbidities, n (%)	78 (27.7)	36 (20.5)	42 (39.6)	$\chi^2=12.15$	<0.001
Diabetes, n (%)	52 (18.4)	26 (14.8)	26 (24.5)	$\chi^2=4.19$	0.041
Linezolid therapy, n (%)	110 (39.0)	110 (62.5)	0 (0)	$\chi^2=108.6$	<0.001

Table 3: Laboratory risk factor univariate analysis of ICU MRSA pneumonia mortality

Variable	Total (n=282)	Survival (n=176)	Death (n=106)	t / Z	P
Albumin (g/L), Mean ± SD	32.57 ± 4.59	33.25 ± 4.44	31.44 ± 4.64	3.26	0.001
PCT, M (Q ₁ –Q ₃)	0.54 (0.22–1.80)	0.36 (0.17–1.16)	1.06 (0.35–3.42)	-4.68	<0.001
CRP (mg/L), M (Q ₁ –Q ₃)	101.7 (50.88–160.90)	91.0 (41.48–146.70)	113.85 (68.0–185.82)	-2.91	0.004
Neutrophil %, M (Q ₁ –Q ₃)	86.95 (82.30–91.10)	85.70 (81.38–90.25)	88.55 (84.20–91.90)	-3.10	0.002
Lymphocyte count, M (Q ₁ –Q ₃)	0.90 (0.60–1.30)	0.90 (0.70–1.30)	0.80 (0.60–1.20)	-2.24	0.025
PT, M (Q ₁ –Q ₃)	12.50 (11.50–13.70)	12.30 (11.40–13.53)	12.85 (11.72–14.20)	-2.37	0.018
CREA, M (Q ₁ –Q ₃)	57.0 (44–77.75)	54.0 (43–71)	63.5 (46–86.75)	-2.34	0.019

Table 4: Multivariate logistic regression analysis of independent risk factors of death among ICU MRSA pneumonia patients

Variable	β	S.E	Z	P	OR (95% CI)
>60 years	0.74	0.31	2.40	0.017	2.09 (1.14–3.81)
Tracheal intubation	1.66	0.41	4.06	<0.001	5.24 (2.36–11.64)
Central venous cannula	0.63	0.32	1.98	0.048	1.87 (1.01–3.47)
≥3 comorbidities	0.91	0.31	2.93	0.003	2.48 (1.35–4.55)
PCT	0.05	0.02	2.54	0.011	1.05 (1.01–1.09)
Linezolid therapy	-1.14	0.33	-3.45	<0.001	0.32 (0.17–0.61)

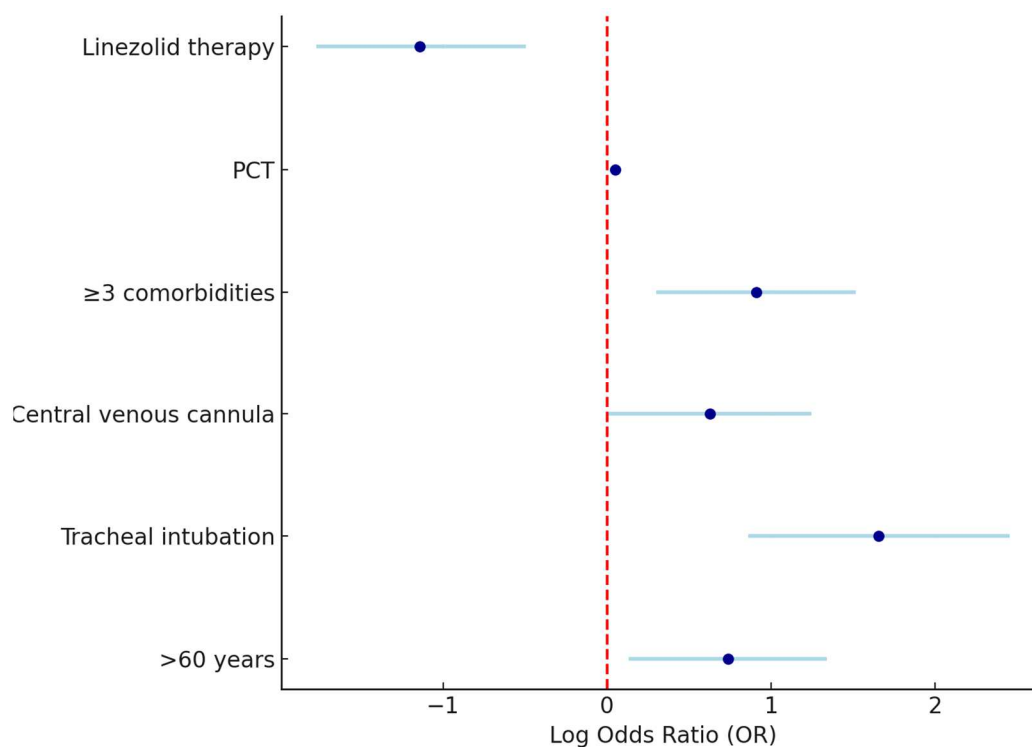


Fig. 1: Independent risk and protective factors for ICU MRSA pneumonia mortality; Red dashed line indicates OR = 1; right-pointing are pro-mortality; linezolid (OR <1) is protective.

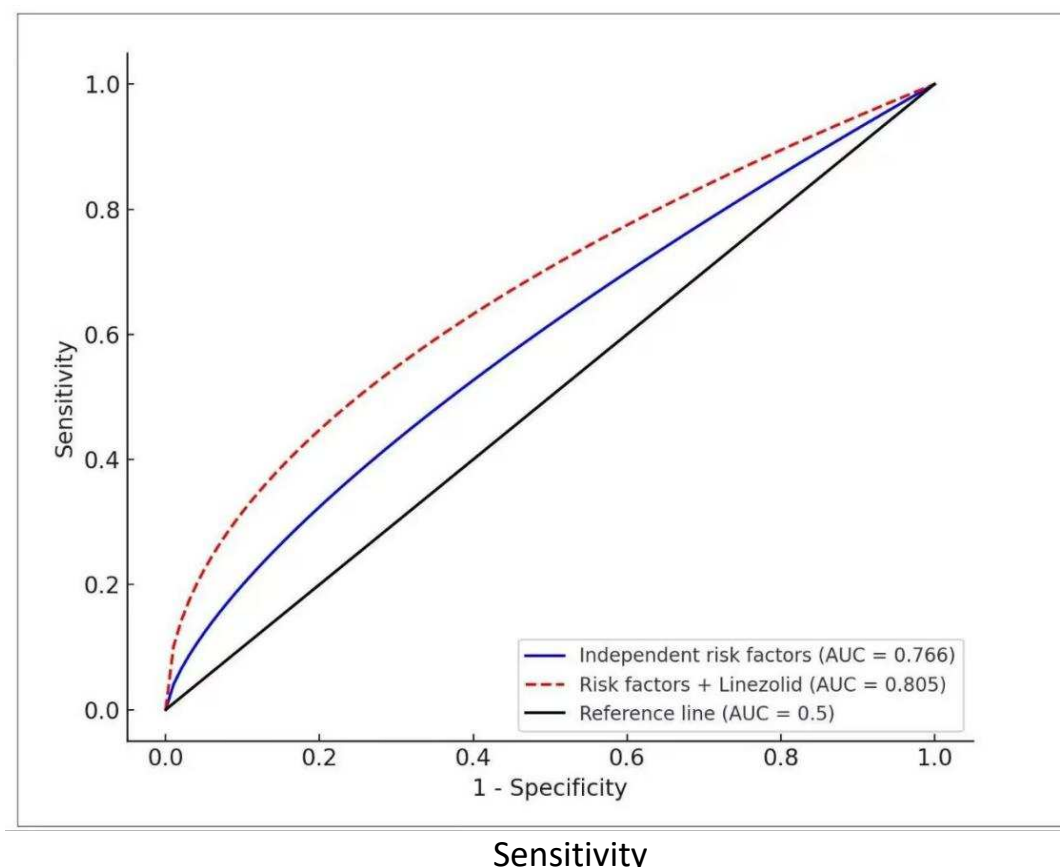


Fig. 2: ROC curves for mortality risk factors with and without linezolid therapy.

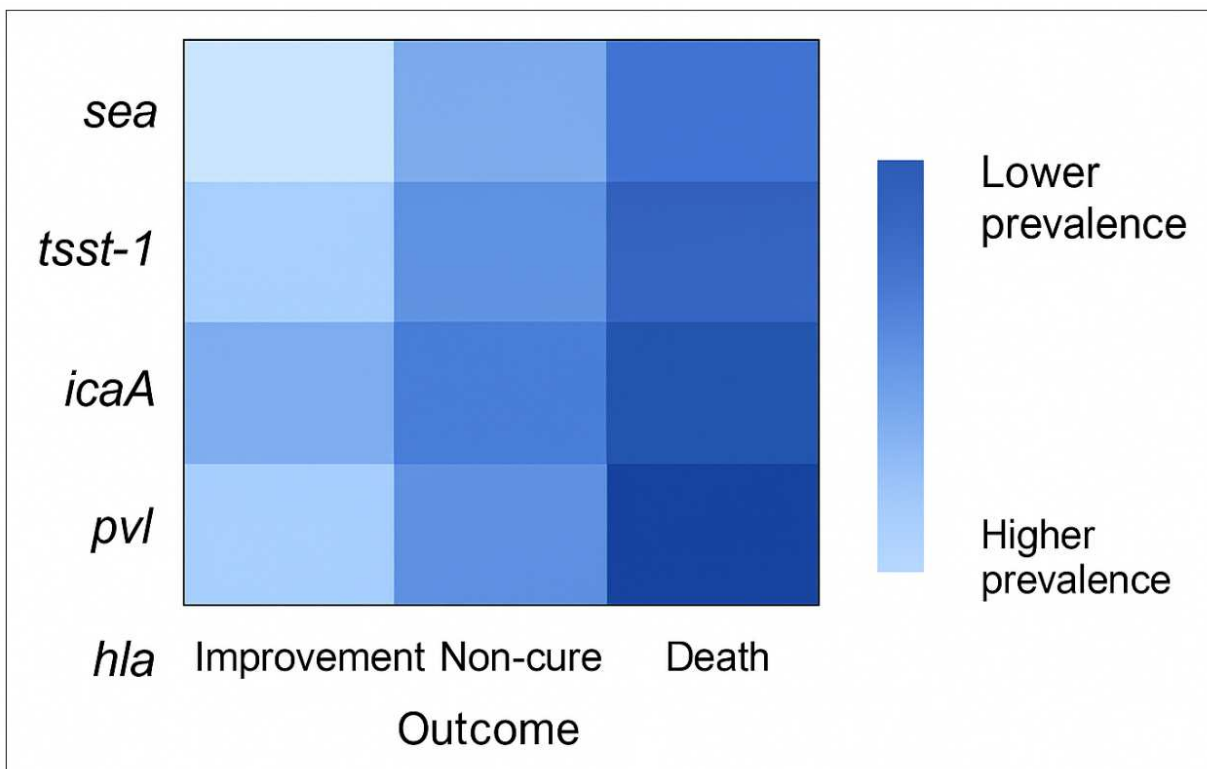


Fig. 3: Heatmap showing virulence gene prevalence in improvement, non-cure and death groups.

In addition, table 7 expands upon the findings of SCCmec genotyping showing the distribution of different SCCmec types that play a key role in the understanding of the molecular epidemiology and resistance mechanisms that are inherent within the MRSA strains.

Distribution of virulence genes and linezolid effect

Sea, tsst-1, icaA and pvl were more present in death and non-cure groups than in linezolid-treated improvement patients (Table 8, Fig. 3). Pvl-positive strains co-carried hla, tsst-1 and icaA with higher frequency (Table 9). Multiple comparisons not adjusted due to exploratory nature.

DISCUSSION

Total mortality among our ICU patients with MRSA pneumonia was 37.6%, congruent with previous Chinese ICU reports (Cilloniz *et al.*, 2021). Univariate analysis demonstrated that greater PCT, CRP and neutrophil levels in the deceased compared to survivors reflected increased infection and systemic inflammatory response (Jones *et al.*, 2020). Malnutrition and hypoproteinemia were predictive as well, since chronic negative nitrogen balance erodes immune competence (Ozdemir *et al.*, 2025; He *et al.*, 2020). Diabetes was another significant risk factor, consistent with earlier research showing diabetic patients to be at increased risk for MRSA infection, more serious pneumonia and higher antimicrobial resistance (Profir *et al.*, 2025; Chung *et al.*, 2021).

Multivariate logistic regression identified age >60 years, tracheal intubation, central venous catheterization, ≥ 3 comorbidities and elevated PCT as independent predictors of mortality (Angioni *et al.*, 2020). Older patients are particularly vulnerable to infection due to compromised immunity and comorbidities with complex pulmonary infections. Invasive interventions such as mechanical ventilation and central venous catheterization increase the risk of bloodstream infection, complicating ICU management (Russo *et al.*, 2023). Although blood transfusion alone was not an independent predictor of mortality, transfused patients tended to have greater PCT values and intubation rates, indicating more severe illness (Schoevaerdt *et al.*, 2021; Zou *et al.*, 2025). The evidence supports the importance of early identification of high-risk patients to guide more vigorous monitoring and supportive therapy.

One of the most important findings of the current study is the association of linezolid treatment with improved outcomes in ICU MRSA pneumonia. The patients treated with linezolid experienced lower mortality and diminished PCT levels compared to those who were not treated. Importantly, linezolid treatment was associated with a lower prevalence of major virulence Genes Sea, tsst-1 and icaA among the MRSA strains, unlike the suppression of gene expression directly. This association is to be interpreted cautiously, considering that the study design is retrospective and the molecular typing was conducted on only 72 isolates, diminishing the statistical power for

Table 5: Transfusion status and linezolid therapy comparison

Variable	Non-transfusion (n=187)	Transfusion (n=95)	P
PCT, M (Q ₁ –Q ₃)	0.48 (0.20–1.27)	0.69 (0.27–3.34)	0.015
>60 years, n (%)	125 (66.8)	60 (63.2)	0.538
Tracheal intubation, n (%)	132 (70.6)	84 (88.4)	<0.001
Central venous intubation, n (%)	122 (65.2)	75 (78.9)	0.018

Table 6: mecA gene and virulence genes prevalence among 72 MRSA strains

Gene	Total (n=72)	Notes
mecA	70 (97.2%)	All groups
sea	61 (84.7%)	Lower prevalence observed in linezolid-treated survivors
hla	68 (94.4%)	No significant difference
tsst-1	62 (86.1%)	Lower prevalence observed in linezolid-treated survivors
icaA	32 (44.4%)	Lower prevalence observed in linezolid-treated survivors
pvl	57 (79.2%)	No significant difference

Table 7: SCCmec genotypes of 72 MRSA strains

Type	n (%)
II	45 (62.5)
III	9 (12.5)
IVa	11 (15.3)
Non-typed	7 (9.7)

Table 8: Virulence gene carriage in improvement (linezolid-treated), non-cure and death groups

Gene	Improvement (n=24)	Non-cure (n=24)	Death (n=24)	P
sea	15 (62.5)	23 (95.8)	23 (95.8)	0.002
hla	20 (83.3)	24 (100)	24 (100)	0.031
tsst-1	14 (58.3)	24 (100)	24 (100)	<0.001
icaA	5 (20.8)	16 (66.7)	11 (45.8)	0.006
pvl	13 (54.2)	21 (87.5)	23 (95.8)	0.001

Table 9: Co-existence between pvl+ and pvl– strains of virulence genes

Gene	pvl+ (n=57)	pvl– (n=15)	P
sea	51 (89.5)	10 (66.7)	0.075
hla	57 (100)	11 (73.3)	0.001
tsst-1	57 (100)	5 (33.3)	<0.001
icaA	31 (54.4)	1 (6.7)	0.001

subgroup analysis. Nevertheless, the reduction in prevalence among linezolid-treated patients of these virulence factors does suggest potential clinical benefit, particularly for pvl-positive strains that were highly prevalent in hla, tsst-1 and icaA co-carrying, highly virulent phenotypes.

Phenotypic and genotypic characterization demonstrated that 97.2% of MRSA isolates were mecA carriers, with the most common being SCCmec type II (62.5%), in accordance with hospital-acquired MRSA strains. Positivity for virulence genes was associated with poor outcomes, validating the incorporation of molecular data with clinical decisions. These findings indicate that linezolid therapy would be valuable not only in bacterial

load reduction but also in the eradication of strains with potentially heightened virulence, but causality can't be determined here (AbdAlhafiz *et al.*, 2023; Gatti *et al.*, 2023; Papan *et al.*, 2021).

The originality of this research involves the integration of clinical observation and molecular science in examining the interplay between antibiotic treatment and bacterial virulence for ICU MRSA pneumonia. Few have investigated survival outcomes and prevalence of virulence genes in a single cohort (Ma *et al.*, 2023). Our findings indicate that use of linezolid is correlated with reduced prevalence of important virulence determinants, potentially providing a mechanistic explanation for enhanced survival in risky patients. These results are

exploratory and hypothesis-generating but not confirmatory, though (Eslami *et al.*, 2025; Cai *et al.*, 2025; Candel *et al.*, 2023).

There are a number of limitations that need to be highlighted. The retrospective design creates potential bias and sputum sample use can result in upper airway colonization contamination, resulting in misclassification. Statistical power in subgroup comparisons was restricted because analysis of virulence genes was done on only a subset of 72 isolates. Prior exposures to antibiotics were recorded but not fully controlled in multivariate models, which resulted in potential confounding. Furthermore, the relative timing of isolate collection with respect to linezolid therapy can influence observed relationships. Follow-up studies must use bronchoalveolar lavage fluid or more uniform specimens for pathogen recovery, enroll larger multicenter populations and harmonize linezolid therapy timing and duration in order to verify these relationships.

Despite these limitations, this study provides clinically relevant information. Independent predictors of mortality, detected together with molecular typing, may assist in early risk stratification and guide the selection of antibiotics. Early initiation of linezolid therapy may be an innovative therapeutic option in severely ill patients with multiresistant MRSA pneumonia. Subsequent research should also examine the optimal timing, length and combination therapy regimens, as well as linezolid's potential immunomodulatory impacts, to continue individualizing care for high-risk ICU patients (Eslami *et al.*, 2025; Cai *et al.*, 2025; Candel *et al.*, 2023).

CONCLUSION

Outcomes of ICU patients with MRSA pneumonia are highly influenced by age, comorbidities, invasive interventions and inflammatory markers. Linezolid therapy was associated with improved survival and reduced frequency of key virulence genes, which holds promising treatment for high-risk patients awaiting confirmation. Early detection of at-risk patients and effective linezolid therapy can improve outcomes and use of clinical and molecular data can allow more individualized therapy for critically ill adults with MRSA pneumonia.

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Authors' contributions

Hu Ren, Liu Guang-zhen contributed to study conceptualization, clinical data collection and interpretation of results. Hu Ren performed microbiological analyses, including DNA extraction, PCR experiments and genotypic characterization of MRSA isolates. Yan Zhen supervised the study, designed the research, analyzed data, drafted the manuscript and served

as the corresponding author. All authors contributed to manuscript revision, approved the final version and are accountable for all aspects of the work.

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Data availability statement

Datasets available from corresponding author on reasonable request; statement added.

Ethical approval

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Xuzhou Medical University Affiliated Hospital (Approval No. XYZ-2024-001). Written informed consent was obtained from all patients or their legal guardians prior to inclusion in the study.

Conflict of interest

The authors declare that they have no conflicts of interest relevant to this study.

REFERENCES

- AbdAlhafiz AI, Elleboudy NS, Aboshanab KM, Aboulwafa MM and Hassouna NA (2023). Phenotypic and genotypic characterization of linezolid resistance and the effect of antibiotic combinations on methicillin-resistant *Staphylococcus aureus* clinical isolates. *Ann. Clin. Microbiol. Antimicrob.*, **22**(1): 23.
- Ali GH and Seiffen NL (2021). Association of some virulence genes in methicillin resistant and methicillin sensitive *Staphylococcus aureus* infections isolated in community with special emphasis on pvl/mecA genes profiles in Alexandria, Egypt. *Gene Rep.*, **25**: 101334.
- Angioni D, Hites M, Jacobs F and De Breucker S (2020). Predictive factors of in-hospital mortality in older adults with community-acquired bloodstream infection. *J. Frailty Aging*, **9**(4): 232-7.
- Cai X, Lin Y, Wu B, Luo Y and Li K (2025). Sputum microbiota profiles of patients with rifampicin-resistant tuberculosis during the intensive-phase treatment. *BMC Microbiol.*, **25**:373.
- Candel FJ, Salavert M, Estella A, Ferrer M, Ferrer R, Gamazo JJ, García-Vidal C, Del Castillo JG, González-Ramallo VJ and Miron-Rubio M (2023). Ten issues to update in nosocomial or hospital-acquired pneumonia: An expert review. *J. Clin. Med.*, **12**(20): 6526.
- Chung H, Kim E, Yang E, Lee YW, Park JH, Bae S, Jung J, Kim MJ, Chong YP, Kim SH and Lee SO (2021). C-reactive protein predicts persistent bacteremia caused by community-acquired methicillin-resistant *Staphylococcus aureus* strain. *Eur. J. Clin. Microbiol. Infect. Dis.*, **40**(12): 2497-504.
- Cilloniz C, Dominedo C, Gabarrus A, Garcia-Vidal C, Becerril J, Tovar D, Moreno E, Pericas JM, Vargass CR

- and Torres A (2021). Methicillin-susceptible *Staphylococcus aureus* in community-acquired pneumonia: risk factors and outcomes. *J. Infect.*, **82**(1): 76-83.
- Dennis LS, Daniel H, Harry L, John LH, Donald HB, Barry H and Linezolid MRSA Study Group (2002). Linezolid versus vancomycin for the treatment of methicillin-resistant *Staphylococcus aureus* infections. *Clin. Infect. Dis.*, **34**(11):1481-90.
- Duraiswamy S, Agarwalla S, Lok KS, Tse YY, Wu R and Wang Z (2023). A multiplex Taqman PCR assay for MRSA detection from whole blood. *PLoS One.*, **18**(11): e0294782.
- Eslami M, Safaripour A, Banihashemian SZ, Nikjoo Niaragh S, Hemmati MA, Shojaeian A, Fakhariyan S, Rabbani A and Oksenykh V (2025). Innovative antibiotic therapies for carbapenem-resistant gram-negative bacterial infections: Clinical efficacy, safety and comparative studies. *Microorganisms.*, **13**(2): 295.
- Gatti M, Viaggi B, Rossolini GM, Pea F and Viale P (2023). Targeted therapy of severe infections caused by *Staphylococcus aureus* in critically ill adult patients: A multidisciplinary proposal of therapeutic algorithms based on real-world evidence. *Microorganisms.*, **11**(2): 394.
- Guo LY, Yan SZ, Tao X, Yang Q, Li Q, Wang TS, Yu SQ and Chen SL (2020). Evaluation of hypocrellin A-loaded lipase sensitive polymer micelles for intervening methicillin-resistant *Staphylococcus aureus* antibiotic-resistant bacterial infection. *Mater Sci. Eng. C.*, **106**: 110230.
- Hayakawa K, Yamaguchi T, Ono D, Suzuki H, Kamiyama J, Taguchi S and Kiyota K (2020). Two cases of intrafamilial transmission of community-acquired methicillin-resistant *Staphylococcus aureus* producing both PVL and TSST-1 causing fatal necrotizing pneumonia and sepsis. *Infect. Drug Resist.*, **13**: 2921-7.
- He H and Wunderink RG (2020). *Staphylococcus aureus* pneumonia in the community. In *Seminars in Respiratory and Critical Care Medicine*, **41**(04): 470-479.
- Hyun H, Song JY, Yoon JG, Seong H, Noh JY, Cheong HJ and Kim WJ (2022). Risk factor-based analysis of community-acquired pneumonia, healthcare-associated pneumonia and hospital-acquired pneumonia: Microbiological distribution, antibiotic resistance and clinical outcomes. *PLoS One.*, **17**(6): e0270261.
- Ibrahim RA, Berhe N, Mekuria Z, Seyoum ET, Balada-Llasat JM, Abebe T, Mariam SH, Tsige E, Fentaw Dinku S and Wang SH (2023). Antimicrobial resistance and virulence gene profile of clinical *Staphylococcus aureus*: A multi-center study from Ethiopia. *Infect Drug Resist.*, **16**: 4835-44.
- Ismael R, Alhameedawi AK, Abbas RS, Alsallameh S, Amer H, Firat M and Karkhane M (2023). Virulence genes and methicillin-resistant gene detection and antimicrobial resistance profiles isolated from different infection sites. *Egypt Pharm. J.*, **22**(2): 265-71.
- Jones BE, Ying J, Stevens V, Haroldsen C, He T, Nevers M, Christensen MA, Nelson RE, Stoddard GJ, Sauer BC and Yarbrough PM (2020). Empirical anti-MRSA vs standard antibiotic therapy and risk of 30-day mortality in patients hospitalized for pneumonia. *JAMA Intern. Med.*, **180**(4): 552-60.
- Kawasuji H, Nagaoka K, Tsuji Y, Kimoto K, Takegoshi Y, Kaneda M, Murai Y, Karaushi H, Mitsutake K and Yamamoto Y (2023). Effectiveness and safety of linezolid versus vancomycin, teicoplanin, or daptomycin against methicillin-resistant *Staphylococcus aureus* bacteremia: A systematic review and meta-analysis. *Antibiotics.*, **12**(4): 697.
- Kohno S, Yamaguchi K, Aikawa N, Sumiyama Y, Odagiri S, Aoki N, Niki Y, Watanabe S, Furue M, Ito T and Croos-Dabrera R (2007). Linezolid versus vancomycin for the treatment of infections caused by methicillin-resistant *Staphylococcus aureus* in Japan. *J Antimicrob. Chemother.*, **60**(6): 1361-9.
- Loaiza WM, Ruiz AK, Patiño CC and Vivas MC (2023). Bacterial resistance in hospital-acquired infections acquired in the intensive care unit: A systematic review. *Acta. Med.*, **66**(1): 1-10.
- Ma A, Dong M, Cheng J, Liao X, Dong W, Liu C, Hu C, Yang J and Kang Y (2023). Clinical efficacy and safety of linezolid in intensive care unit patients. *J. Intensive Med.*, **3**(1):65-72.
- Moazen J, Zaniani FR and Asghar BH (2022). Characterization of virulence genes and antibiotic resistance of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *Staphylococcus aureus* (MSSA) isolates in intensive care unit (ICU) and non-ICU wards. *Trends Med. Sci.*, **2**(2): e129037.
- Ozdemir Y, Kaya NF, Ari A, Tosun S, Çalık Ş and Bayram ED (2025). Predictors of mortality in *Staphylococcus aureus* infections: The role of C-reactive protein, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio. *J. Int. Med. Res.*, **53**(8): 03000605251363105.
- Papan C, Schroder M, Hoffmann M, Knoll H, Last K, Albrecht F, Geisel J, Fink T, Gartner BC, Mellmann A and Volk T (2021). Combined antibiotic stewardship and infection control measures to contain the spread of linezolid-resistant *Staphylococcus epidermidis* in an intensive care unit. *Antimicrob. Resist Infect. Control.*, **10**(1): 99.
- Peng Z, Zhou JA and Tian L (2020). Pathogenic characteristics of sputum and bronchoalveolar lavage fluid samples from patients with lower respiratory tract infection in a large teaching hospital in China: A retrospective study. *BMC Pulm. Med.*, **20**(1): 233.
- Pichon M, Micaelo M, Rasoanandrasana S and Menn AM (2021). Molecular characterization of *Staphylococcus aureus* isolates derived from severe pneumonia: A

- retrospective monocentre study. *Infect Dis.*, **53**(11): 811-9.
- Pickens CI and Wunderink RG (2022). Methicillin-resistant *Staphylococcus aureus* hospital-acquired pneumonia/ventilator-associated pneumonia. In *Seminars Respir Crit. Care Med.*, **43**(02): 304-309.
- Profir I, Popescu CM and Nechita A (2025). Fatal influenza B–MRSA coinfection in a healthy adolescent: Necrotizing pneumonia, Cytokine storm and multi-organ failure. *Children.*, **12**(6): 766.
- Rao GG, Konicki R, Cattaneo D, Alffenaar JW, Marriott DJ, Neely M and IATDMCT Antimicrobial Scientific Committee (2020). Therapeutic drug monitoring can improve linezolid dosing regimens in current clinical practice: A review of linezolid pharmacokinetics and pharmacodynamics. *Ther. Drug Monit.*, **42**(1): 83-92.
- Rongrungruang Y, Plongla R, Pleumkanitkul S, Hantrakun V and Khawcharoenporn T (2025). Etiology of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) in tertiary-care hospitals in Thailand: A multicenter, retrospective cohort study. *Infect. Drug Resist.*, **18**: 351-61.
- Russo A, Salini S, Gava G, Merra G, Piccioni A, De Matteis G, Tullo G, Novelli A, Petrucci M, Gasbarrini A and Landi F (2023). Reduced prognostic role of serum PCT measurement in very frail older adults admitted to the emergency department. *Antibiotics.*, **12**(6): 1036.
- Schoevaerds D, Sibille FX and Gavazzi G (2021). Infections in the older population: What do we know?. *Aging Clin. Exp. Res.*, **33**(3): 689-701.
- Shi Y, Wu HL, Wu YH, Li S, Zhang LY, Xu SS, Huang HY, Zhang CH, Yu XB, Cai K and Zhang J (2023). Safety and clinical efficacy of linezolid in children: A systematic review and meta-analysis. *World J. Pediatr.*, **19**(2): 129-38.
- Silva V, Almeida L, Gaio V, Cerca N, Manageiro V, Caniça M, Capelo JL, Igrejas G and Poeta P (2021). Biofilm formation of multidrug-resistant MRSA strains isolated from different types of human infections. *Pathogens.*, **10**(8): 970.
- Solmaz I and Kalın BS (2021). Assessment of antibiotic resistance of infectious agents in patients with pneumonia in tertiary critical care unit and effect on clinical outcomes. *Int. J. Clin. Pract.*, **75**(4): e13872.
- Touaitia R, Mairi A, Ibrahim NA, Basher NS, Idres T and Touati A (2025). *Staphylococcus aureus*: A review of the pathogenesis and virulence mechanisms. *Antibiotics.*, **14**(5): 470.
- Vo-Pham-Minh T, Tran-Cong D, Phan-Viet H, Dinh-Chi T, Nguyen-Thi-Hong T, Cao-Thi-My T, Nguyen-Thi-Dieu H, Vo-Thai D, Nguyen-Thien V and Duong-Quy S (2024). *Staphylococcus aureus* pneumonia in Can Tho, Vietnam: Clinical characteristics, antimicrobial resistance profile and risk factors of mortality. *Pulm. Ther.*, **10**(2): 193-205.
- Watkins RR, Lemonovich TL and File TM Jr (2012). An evidence-based review of linezolid for the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA): Place in therapy. *Core Evid.*, **7**: 131-43.
- Yayan J, Ghebremedhin B and Rasche K (2015). No outbreak of vancomycin and linezolid resistance in *Staphylococcal pneumonia* over a 10-year period. *PLoS One.*, **10**(9): e0138895.
- Zou J, Xiao Y, Zhang L, Zuo Z, Wang X, Liao X, Cui N, Jin J, Qian Z, Wu A and Li C (2025). Enhanced insights into immunity traits of elderly patients in the intensive care unit with infections: Evidence from a multicenter, prospective observational study. *Crit. Care.*, **29**(1): 386.