Original Article

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Clinical Characteristics and Factors Associated with 30-Day Mortality in Patients with Methicillin-resistant Staphylococcal Pneumonia

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Abstract:

Objective: We aimed to identify the risk factors associated with 30-day mortality in patients with methicillin-resistant *Staphylococcus spp.* (MRS) pneumonia.

Material and Methods: From March 2021 to March 2023, we conducted a prospective, observational study at Cho Ray Hospital, Viet Nam, in hospitalized patients aged ≥18 years with pneumonia due to MRS. To assess the risk factors for 30-day mortality, we performed univariable and multivariable logistic regression analyses.

Results: The 30-day mortality was 39.1% (36 out of 92 patients with MRS pneumonia). The risk factors for death within 30 days in cases with MRS pneumonia were severe pneumonia, being overweight, respiratory failure, shock, or having a medical device (a tracheostomy or endotracheal tube, a central venous catheter, a urinary catheter, or a nasogastric tube). The 30-day mortality increased proportionally with the number of risk factors.

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Conclusion: Pre-existing factors were associated with the 30-day mortality risk of MRS pneumonia. Therefore, comprehensive therapy, including initial anti-MRS treatment, might be important for improving outcomes in patients with the studied risk factors.

Keywords: pneumonia, methicillin-resistant *Staphylococcus spp*, 30-day mortality, risk factors

Introduction

Pneumonia is the most common cause of death from infectious diseases worldwide[1,2]. In hospital settings, the mortality rate for pneumonia ranges from 3% to 25%. Notably, the mortality rate can exceed 30% if a patient is admitted to an intensive care unit[3,4]. Methicillin-resistant *Staphylococcus aureus* (MRSA) is associated with significant morbidity and with a 30-day death rate ranging from 10% to 41%[5–7]. Various studies have identified several risk factors that may influence MRSA mortality within 30 days, including age, comorbidities, respiratory failure, shock at admission, multilobar pneumonia, and discordant empiric antibiotic therapy[4,6,8].

Coagulase-negative staphylococci (CoNS), especially methicillin-resistant coagulase-negative staphylococci (MRCoNS), which are recognized as opportunistic pathogens, represent a major group of nosocomial pathogens[9–11]. In 2023, besides MRSA, the Centers for Disease Control and Prevention recommended that CoNS should also be considered a pneumonia pathogen[12].

To improve a patient's prognosis, it is important to identify particular risk factors for MRSA and MRCoNS in pneumonia. We, therefore, conducted this research to identify outcomes and factors associated with the 30-day mortality rate of patients with MRS pneumonia.

Material and Methods

Study design and participants

We conducted a prospective observational study on patients diagnosed with pneumonia at Cho Ray Hospital, Vietnam, from March 2021 to March 2023. Cho Ray Hospital is a tertiary hospital in Southern Vietnam and has approximately 3,000 beds with over 30 clinical departments. The presence of MRS infection in the patients involved in this study was confirmed through either culture or real-time polymerase chain reaction (PCR). Our study included individuals aged 18 years or older who developed pneumonia, including cases of community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP).

Data collection

The data collected included demographic factors, clinical, laboratory, and radiographic findings, treatment therapies and treatment outcomes.

Treatment outcomes (survivors or non-survivors) were collected from the discharge summary or a follow-up phone call to family members.

The risk factors associated with mortality in the study population included a variety of demographic characteristics, comorbid conditions, exposure to antibiotics within the last 90 days, history of MRSA infection, severe sepsis requiring vasopressor support, clinical presentations, laboratory values, chest x-rays and antibiotic therapies prescribed during the admission.

Microbiology methods

Staphylococcus spp. were identified by the VITEK 2 Compact or VITEK MS system. Antibiotic susceptibility testing was performed according to the Clinical and Laboratory Standards Institute guidelines 2020. Real-time

PCRs were done using the MRSA Quant Real-TM kit (Sacace Biotechnologies, Italy)[13].

Definitions

Pneumonia was defined by a new lung infiltrate plus clinical evidence that the infiltrate was of an infectious origin. The presence of a new or progressive radiographic infiltrate plus clinical features (fever, leukocytosis or leukopenia, dyspnea and purulent secretions) as defined in an earlier study was used as the most accurate combination of criteria for starting empiric antibiotic therapy[7,14,15]. CAP, HAP, and VAP were defined using previously published criteria[12,15].

Severe pneumonia was defined by the following criteria: (1) the presence of at least one major criterion, such as the need for invasive mechanical ventilation or septic shock; (2) the presence of three or more minor criteria, including a respiratory rate of ≥30 breaths/min, PaO2/FiO2 ratio ≤250 mmHg, multilobar infiltrates, confusion or disorientation, blood urea nitrogen ≥20 mg/dL, leucopenia, thrombocytopenia, hypothermia, or hypotension requiring aggressive fluid resuscitation[15].

MRS was considered the etiologic agent when confirmed by real-time PCR or when antimicrobial susceptibility testing was conducted using broth microdilution in accordance with the Clinical and Laboratory Standards Institute guidelines[7]. For clinical purposes, a positive MRS result was defined as one that was evident in the initial microbiology test from either blood or a respiratory source (such as sputum, endotracheal aspirate, bronchoalveolar lavage, or pleura)[7,16].

A case of MRS pneumonia was defined as an illness compatible with pneumonia in which MRS was isolated from a respiratory source (sputum, endotracheal aspirate, bronchoalveolar lavage, or pleura or blood in an inpatient setting)[8].

30-day mortality was defined as documented death from any cause within 30 days of a patient being diagnosed with pneumonia[7,8,17].

Anti-MRS antibiotics included vancomycin, linezolid, or teicoplanin. Initial anti-MRS antibiotic referred to the administration of one within the first 48 hours after the diagnosis of pneumonia[7,17,18].

Statistical analysis

We summarized the data using descriptive statistics. We used univariable and multivariate logistic regression analyses to identify factors associated with mortality. The univariate analysis included the following variables: sex, age, comorbidities, physical findings, laboratory and radiographic results, and initial antibiotic therapy. Variables with a p-value<0.05 from the univariable model were included in the final multivariable regression model. The adjusted odds ratios (aORs) as well as 95% confidence intervals (CIs), were calculated. A p-value<0.05 was considered to indicate statistical significance. All statistical analyses were performed using the R Studio program version 4.2.3.

Ethics approval and informed consent

This study was approved by the University of Medicine and Pharmacy in Ho Chi Minh City, approval number 196/HĐĐĐ-ĐHYD. Patient written consent was obtained before the primary collection of individual patient data. All personally identifiable information, including the patient's name and national identification number, was encrypted for storage and de-identification after completing the data collection.

Results

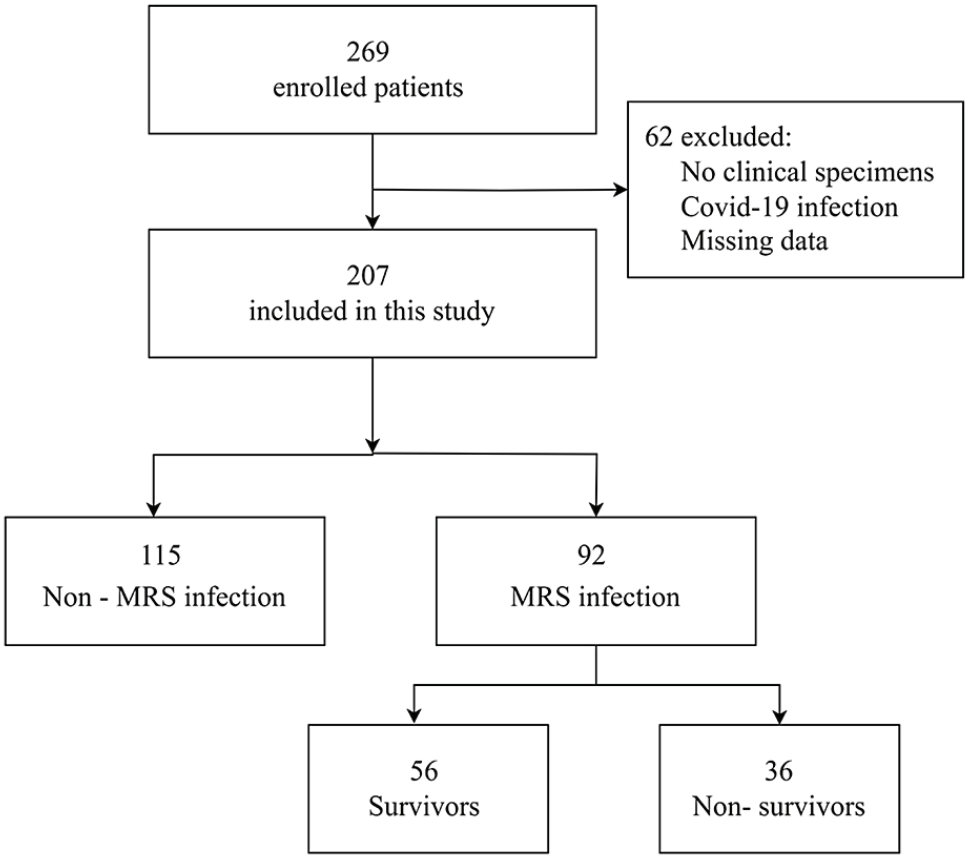
Patient characteristics and 30-day mortality

A total of 207 pneumonia patients underwent eligibility assessment, of whom 92 cases were infected with methicillin-resistant Staphylococcus spp. (Figure 1 and Table 1). Table 1 provides baseline characteristics, identified pathogens, and antibiotic treatments among the patients. The 30-day mortality was 39.1% (36/92) in the MRS pneumonia patients.

Risk factors associated with 30-day mortality in patients with MRS pneumonia.

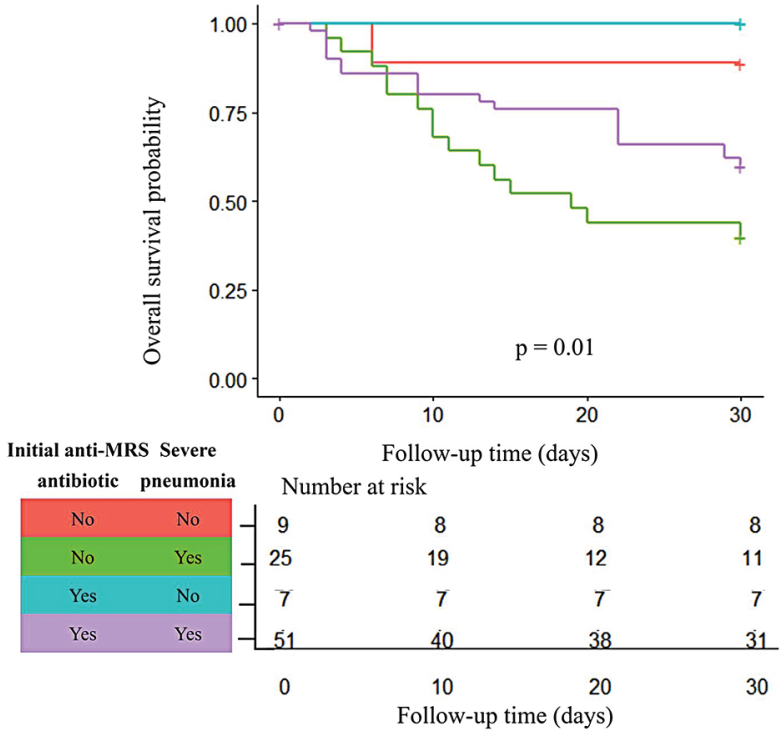
Figure 2 shows the survival curves and frequency distributions of the survivors following the initial anti-MRS antibiotic over time. Patients not receiving initial anti-MRS antibiotics had significantly worse 30-day outcomes (p-value=0.01).

The association between clinical features and 30-day mortality is shown in Table 2. Having severe pneumonia, being overweight, respiratory failure, shock, or having a medical device (a tracheostomy or endotracheal tube, a central venous catheter, a urinary catheter, or a nasogastric tube) were all risk factors for death within 30 days (p-value<0.05 in univariate analysis) (Table 2). However, multivariable regression analysis (Table 3) showed that these risks were not significant independent factors in mortality within 30 days, except for the presence of a tracheostomy or endotracheal tube. Furthermore, a higher number of risk factors was associated with increased 30-day mortality rates (Figure 3A), particularly in patients with two or more risk factors (Figure 3B).



MRSA=methicillin-resistant *Staphylococcus* aureus., MRS=methicillin-resistant *Staphylococcus spp.*

Figure 1 Study flow chart of patients with pneumonia



MRS=methicillin-resistant *Staphylococcus spp.*, non-MRS=non-methicillin-resistant *Staphylococcus spp.*

Figure 2 Distribution of 30-day mortality depending on receiving initial anti-MRS antibiotic in pneumonia

Table 1 Patient characteristics and outcomes

Characteristic	Number of patients (n=207)	Rate (%)
Demographic factors		
Male gender	146	70.5
Age		
Years. mean±S.D.	60.5±16.0	
≥60 years	116	56.0
Types of nosocomial pneumonia		
HAP	113	54.6
VAP	31	15.0
CAP	63	30.4
Bacteraemia		
Non-MRS	115	55.6
MRS	92	44.4
Antibiotic therapy		
Anti-MRS antibiotics	147	71.0
Standard antibiotics	207	100.0
30-day mortality	71	34.3

S.D.=*standard deviation*, HAP=hospital-acquired pneumonia, VAP=*ventilator-associated pneumonia,* CAP=community-acquired pneumonia, MRS=methicillin-resistant *Staphylococcus spp.*

Table 2 Survivor and non-survivor rates by clinical characteristics of the study patients with MRS pneumonia

Variable	Survivors (n=56)	Non-survivors (n=36)	p-value
Sex			
Female	18 (32.1)	10 (27.8)	0.832
Male	38 (67.9)	26 (72.2)	
Age			
Under 60	25 (44.6)	14 (38.9)	0.742
Above 60	31 (55.4)	22 (61.1)	
Age (years, mean±S.D.)	59.5±18.3	62.8±12.6	0.306
BMI			
Underweight	18 (32.1)	6 (16.7)	0.160
Normal range	23 (41.1)	17 (47.2)	0.715
Overweight	6 (10.7)	12 (33.3)	0.016
Obese	9 (16.1)	1 (2.8)	0.098
Type of nosocomial pneumonia			
HAP	31 (55.4)	15 (41.7)	0.334
VAP	7 (12.5)	8 (22.2)	
CAP	18 (32.1)	13 (36.1)	
Comorbidities			
Myocardial infarction	2 (3.6)	1 (2.8)	1.0
Congestive heart failure	8 (14.3)	4 (11.1)	0.901
Peripheral vascular disease	1 (1.8)	0 (0.0)	1.0
Solid tumor	3 (5.4)	2 (5.6)	1.0
Cerebrovascular disease	0 (0.0)	2 (5.6)	0.293
Ulcer disease	4 (7.1)	3 (8.3)	1.0
Diabetes	11 (19.6)	4 (11.1)	0.428
Chronic obstructive pulmonary disease	10 (17.9)	4 (11.1)	0.561
Moderate or severe renal disease	8 (14.3)	7 (19.4)	0.715
Diabetes with complications	12 (21.4)	10 (27.8)	0.655
Hemiplegia	5 (8.9)	2 (5.6)	0.847
Moderate or severe liver disease	5 (8.9)	3 (8.3)	1.0
Metastatic solid tumor	1 (1.8)	3 (8.3)	0.328
AIDS	2 (3.6)	1 (2.8)	1.0
Commodity Channel Index	2 (0-6)	2 (0.0-7.3)	0.524
Previously infected with MRSA	4 (7.1)	1 (2.8)	0.667
Prior intravenous antibiotic use within 90 days	45 (80.4)	29 (80.6)	1.0
Immunodeficiency	9 (16.1)	8 (22.2)	0.641
Severe pneumonia	41 (73.2)	35 (97.2)	0.007
Fever	2 (3.6)	6 (16.7)	0.072
Skin infection	24 (42.9)	14 (38.9)	0.873
Respiratory failure	40 (71.4)	35 (97.2)	0.005
Shock	5 (8.9)	11 (30.6)	0.017
Tracheostomy tube or endotracheal tube	18 (32.1)	31 (86.1)	<0.001
Central venous catheterization	23 (41.1)	24 (66.7)	0.029
Urinary catheterization	20 (35.7)	26 (72.2)	0.001
Nasogastric intubation	21 (37.5)	28 (77.8)	<0.001
Pleural drainage	5 (8.9)	5 (13.9)	0.687
Consolidation	54 (96.4)	34 (94.4)	1.0
Pulmonary cavities	4 (7.1)	3 (8.3)	1.0
Pneumatoceles	10 (17.9)	5 (13.9)	0.831
Pleural effusion	32 (57.1)	19 (52.8)	0.844

Table 2 (continued)

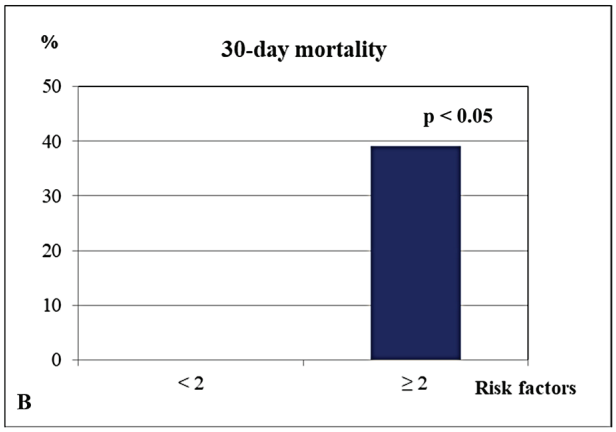
Variable	Survivors (n=56)	Non-survivors (n=36)	p-value
WBC, count/mm^3, mean±S.D.	15.4±6.7	14.9±7.2	0.701
Neutrophils, median and (2.5th-97.5th) percentiles	11.8 (4.2-26.9)	12.7 (2.7-26.0)	0.734
Initial anti-MRS antibiotic	38 (67.9)	20 (55.6)	0.331

S.D.=standard deviation, HAP=hospital-acquired pneumonia, VAP=ventilator-associated pneumonia, CAP=community-acquired pneumonia, BMI=body mass index, AIDS=acquired immunodeficiency syndrome, WBC=white blood cell, MRS=methicillin-resistant *Staphylococcus spp*.

Table 3 Risk factors predictive of MRS pneumonia by multivariate logistic regression

Characteristic	aORs	95% CI	p-value
Age	1.02	0.98-1.06	0.327
Overweight	3.08	0.85-12.72	0.097
Severe pneumonia	4.25	0.33-200.27	0.344
Respiratory failure	5.27	0.50-198.51	0.238
Shock	1.76	0.42-8.14	0.450
Tracheostomy tube or endotracheal tube	5.42	1.32-25.55	0.023
Central venous catheterization	0.35	0.05-1.86	0.244
Nasogastric intubation	6.94	0.52-220.40	0.177
Urinary catheterization	0.37	0.01-4.17	0.465

MRS=methicillin-resistant *Staphylococcus spp*, aORs=adjusted odds ratios, 95% CI= 95% confidence interval



	Number of risk factors	Total (n = 92)	30-day mortality (n = 92)
A	0-1	14 (15.2)	0 (0)
	2	14 (15.2)	1 (1.1)
	3	14 (15.2)	5 (5.4)
	≥ 4	50 (54.3)	30 (32.6)

MRS=methicillin-resistant *Staphylococcus spp*.

Figure 3 30-day mortality in MRS pneumonia patients with different numbers of risk factors

Discussion

To find out factors associated with 30-day mortality in the study patients with MRS pneumonia, we analyzed (1) the rate of 30-day mortality in MRS pneumonia patients and (2) several risk factors associated with 30-day mortality, including demographic factors, comorbidities, clinical symptoms, laboratory findings, image features, and anti-MRS antibiotic therapy.

MRSA and MRCoNS have been recognized as serious pathogens in pneumonia[12,15,19-21]. Nowadays, Methicillin-resistant staphylococcal pneumonia has become an increasing concern worldwide because it is associated with high overall mortality and multiple antibiotic resistance[1,4,5,7,11]. The 30-day all-cause mortality rate ranges from 28% to 41%[5,7,11]. The frequency of this mortality increases with age, comorbidities, severe pneumonia, and complications[6,7,14]. Therefore, early recognition of MRS infections and evaluation of factors influencing mortality are crucial for improving patient outcomes.

In this study, we examined the risk factors for 30-day mortality in patients with MRS pneumonia. The independent risk factors were severe pneumonia, being overweight, respiratory failure, shock, or having a medical device (a tracheostomy or endotracheal tube, a central venous catheter, a urinary catheter, or a nasogastric tube) (Table 2). Patients with two risk factors had a substantially higher 30-day mortality (Figure 3). Therefore, the presence of 2 or more risk factors at diagnosis was a predictor of adverse outcomes[18] .

Comprehensive treatments would be needed to improve the outcomes in patients with MRS pneumonia[7], such as appropriate initial antibiotics and other adjunctive therapies[22]. Currently, recommended initial antibiotics for probable MRS pneumonia are vancomycin, linezolide, or teicoplanin[17,23]. Table 2 shows the adverse association our study found concerning medical devices on patient mortality, which suggests the benefits of early removal of unnecessary medical devices (tracheostomy or endotracheal tubes, central venous catheters, urinary catheters, or nasogastric tubes)[24]. Also, clinical signs of treatment failure for MRS pneumonia, such as fever, respiratory failure, or shock, should prompt repetitions of microbiology tests to help guide the choice of definite therapy[24].

The findings of our study carry potential implications for MRS pneumonia management. The 30-day mortality in our study patients with MRS pneumonia was high. Timely interventions in patients with many risk factors, such as removing medical devices and anti-MRS antibiotic therapy, may significantly contribute to achieving better outcomes. Our study had several limitations. First, we assessed the 30-day all-cause mortality as the endpoint. However, causes of death can include other comorbid diseases such as cardiac diseases or neurologic diseases. Second, detailed information about adjunctive therapies was not obtained. Third, other microbiological factors we did not cover could affect mortality; therefore, further studies of the assessment of comorbidities, microbiological factors, and adjunctive therapies for these risk factors need to be done.

Conclusion

Respiratory failure, shock, or having a medical device were all risk factors for death within 30 days in patients with MRS pneumonia. For patients with two or more risk factors, initiating anti-MRS antibiotic therapy and providing comprehensive care are necessary.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Contributions

All the authors made a substantive intellectual contribution. All the authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

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Conflict of interest

There are no potential conflicts of interest to declare.

References

1. Chansareewittaya K, Krajangcharoensakul S. The occurrence of antibiotic resistant bacteria contamination in sub-district health-promoting hospitals in Chiang Rai, Thailand. J Health Sci Med Res 2022;40:459-73. doi: 10.31584/jhsmr.2021857.
2. World Health Organization. WHO reveals leading causes of death and disability worldwide: 2000-2019. [homepage on the Internet]. Geneva: WHO; 2020 [cited 2024 Jan 18]. Available from: https://www.who.int/news/item/09-12-2020-who-reveals-leading-causes-of-death-and-disability-worldwide-2000-2019.
3. Kang SY, Cha WC, Yoo J, Kim T, Park JH, Yoon H, et al. Predicting 30-day mortality of patients with pneumonia in an emergency department setting using machine-learning models. Clin Exp Emerg Med 2020;7:197-205. doi: 10.15441/ceem.19.052.
4. Garcia-Vidal C, Fernández-Sabé N, Carratalà J, Díaz V, Verdaguer R, Dorca J. Early mortality in patients with community-acquired pneumonia: causes and risk factors. Eur Respir J 2008;32:733-9. doi: 10.1183/09031936.00128107.
5. Lee LN, Chou WR, Wang JY, Wang JY, Kuo YL, Chang CY, et al. Characteristics and local risk factors of community-acquired and health-care-associated Staphylococcus aureus pneumonia. Sci Rep 2022;12:18670. doi: 10.1038/s41598-022-23246-1.
6. Thabet N, Shindo Y, Okumura J, Sano M, Sakakibara T, Murakami Y et al. Clinical characteristics and risk factors for mortality in patients with community-acquired staphylococcal pneumonia. Nagoya J Med Sci 2022;84:247-59. doi: 10.18999/nagjms.84.2.247.
7. Tadros M, Williams V, Coleman BL, McGeer AJ, Haider S, Lee C, et al. Epidemiology and outcome of pneumonia caused by methicillin-resistant *Staphylococcus aureus* (MRSA) in Canadian hospitals. PLoS One 2013;8:e75171. doi: 10.1371/journal.pone.0075171.
8. Jones BE, Ying J, Stevens V, Haroldsen C, He T, Nevers M, et al. Empirical anti-MRSA vs standard antibiotic therapy and risk of 30-day mortality in patients hospitalized for pneumonia. JAMA Intern Med 2020;180:552-60. doi: 10.1001/jamainternmed.2019.7495.
9. Carretto E, Barbarini D, Couto I, De Vitis D, Marone P, Verhoef J, et al. Identification of coagulase-negative staphylococci other than *Staphylococcus epidermidis* by automated ribotyping. Clin Microbiol Infect 2005;11:177-84. doi: 10.1111/j.1469-0691.2004.01052.x.
10. Pfaller MA, Herwaldt LA. Laboratory, clinical, and epidemiological aspects of coagulase negative staphylococci. Clin Microbiol Rev 1988;1:281-99.
11. Demiselle J, Meyer P, Lavigne T, Kaurin J, Merdji H, Schenck M, et al. Clinical research in intensive care and sepsis – trial group for global eval-¨. *Staphylococcus epidermidis* bloodstream infections are a cause of septic shock in ICU patients. Int J Infect Dis 2023:00665-3. doi: 10.1016/j.ijid.2023.07.014.
12. National Healthcare Safety Network. Pneumonia (Ventilatorassociated [VAP] and non-ventilator-associated Pneumonia [PNEU]) Events. [homepage on the Internet]. CDC; National Healthcare Safety Network; 2024 [cited 2024 Apr 3]. Available from: https://www.cdc.gov/nhsn/pdfs/pscmanual/6pscvapcurrent.pdf.
13. Mutonga DM, Mureithi MW, Ngugi NN, Otieno FCF. Bacterial isolation and antibiotic susceptibility from diabetic foot ulcers in Kenya using microbiological tests and comparison with RT-PCR in detection of *S. aureus* and MRSA. BMC Res Notes 2019;12:244. doi: 10.1186/s13104-019-4278-0.
14. Vardakas KZ, Matthaiou DK, Falagas ME. Incidence, characteristics and outcomes of patients with severe community acquired-MRSA pneumonia. Eur Respir J 2009;34:1148-58. doi: 10.1183/09031936.00041009.
15. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K,et al. Diagnosis and treatment of adults with community-acquired pneumonia. an official clinical practice guideline of

the american thoracic society and infectious diseases society of America. Am J Respir Crit Care Med 2019;200:e45-67. doi: 10.1164/rccm.201908-1581ST.

16. Li R, Tang H, Xu H, Cui K, Li S, Shen J. Effect on 30-day mortality and duration of hospitalization of empirical antibiotic therapy in CRGNB-infected pneumonia. Ann Clin Microbiol Antimicrob 2021;20:15. doi: 10.1186/s12941-021-00421-2.
17. Shime N, Saito N, Bokui M, Sakane N, Kamimura M, Shinohara T, et al. Clinical outcomes after initial treatment of methicillin-resistant *Staphylococcus aureus* infections. Infect Drug Resist 2018;6:1073-81. doi: 10.2147/IDR.S159447.
18. Shindo Y, Ito R, Kobayashi D, Ando M, Ichikawa M, Goto Y, et al. Risk factors for 30-day mortality in patients with pneumonia who receive appropriate initial antibiotics: an observational cohort study. Lancet Infect Dis 2015;15:1055-65. doi: 10.1016/S1473-3099(15)00151-6.
19. Becker K, Heilmann C, Peters G. Coagulase-Negative Staphylococci. Clinical Microbiology Reviews 2014:870-926. doi: 10.1128/CMR.00109-13.
20. Michels R, Last K, Becker SL, Papan C. Update on Coagulase-Negative Staphylococci—What the Clinician Should Know. Microorganisms 2021:9:830.
21. Michalik M, Samet A, Podbielska-Kubera A, Savini V, Międzobrodzki J, Kosecka-Strojek M, et al. Coagulase-negative staphylococci (CoNS) as a significant etiological factor of laryngological infections: a review. Ann Clin Microbiol Antimicrob 2020:19:26. doi: 10.1186/s12941-020-00367-x.
22. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013;41:580-637. doi: 10.1097/CCM.0b013e31827e83af.
23. Ju G, Zhang Y, Ye C, Liu Q, Sun H, Zhang Z, et al. Comparative effectiveness and safety of six antibiotics in treating MRSA infections: a network meta-analysis. Int J Infect Dis 2024;146: 107109. doi: 10.1016/j.ijid.2024.107109.
24. Brown NM, Goodman AL, Horner C, Jenkins A, Brown EM. Treatment of methicillin-resistant *Staphylococcus aureus* (MRSA): updated guidelines from the UK. JAC Antimicrob Resist 2021;3:dlaa114. doi: 10.1093/jacamr/dlaa114.