

Severe Pneumonia Caused by *Corynebacterium striatum* in Adults, Seoul, South Korea, 2014–2019

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Learning Objectives

Upon completion of this activity, participants will be able to:

- Assess the proportion, demographics, underlying diseases, and pathogens of severe *Corynebacterium striatum* hospital-acquired pneumonia in adults compared with those of severe methicillin-resistant *Staphylococcus aureus* hospital-acquired pneumonia, based on a retrospective study
- Evaluate the clinical characteristics, laboratory findings, and outcomes of severe *Corynebacterium striatum* hospital-acquired pneumonia in adults compared with those of severe methicillin-resistant *Staphylococcus aureus* hospital-acquired pneumonia, based on a retrospective study
- Determine the clinical implications of the proportion, clinical characteristics, and outcomes of severe *Corynebacterium striatum* hospital-acquired pneumonia in adults compared with those of severe methicillin-resistant *Staphylococcus aureus* hospital-acquired pneumonia, based on a retrospective study

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We investigated the proportion and characteristics of severe *Corynebacterium striatum* pneumonia in South Korea during 2014–2019. As part of an ongoing observational study of severe pneumonia among adult patients, we identified 27 severe *C. striatum* pneumonia cases. Most (70.4%) cases were hospital-acquired, and 51.9% of patients were immunocompromised. *C. striatum* cases among patients with severe hospital-acquired pneumonia (HAP) increased from 1.0% (2/200) during 2014–2015 to 5.4% (10/185) during 2018–2019, but methicillin-resistant *Staphylococcus aureus* (MRSA) infections among severe HAP cases decreased from 12.0% to 2.7% during the same timeframe. During 2018–2019, *C. striatum* was responsible for 13.3% of severe HAP cases from which bacterial pathogens were identified. The 90-day mortality rates were similarly high in the *C. striatum* and MRSA groups. *C. striatum* was a major cause of severe HAP and had high mortality rates. This pathogen is emerging as a possible cause for severe pneumonia, especially among immunocompromised patients.

Corynebacterium striatum is a nonlipophilic, fermentative coryneform bacterium that commonly occupies the normal flora of the skin and oropharynx (1). Although *C. striatum* isolated from clinical specimens has frequently been considered a contaminant, it is increasingly recognized as a pathogen of various infections, including central line-associated bacteremia (2), endocarditis (3), and pleuropulmonary infection (4–6). In 1980, *C. striatum* was reported as a cause of pleuropulmonary infection in a patient with chronic lymphocytic leukemia (4). In 2018, a group of researchers in the United States reported 3 cases of community-acquired pneumonia (CAP) in which *Corynebacterium* species were the predominant isolate and suggested that *Corynebacterium* species are a noteworthy clinical cause of pneumonia (6). However, scarce information is available on the incidence, clinical characteristics, and outcomes of severe *C. striatum* pneumonia in critically ill adult patients, because previous studies included ≤ 5 patients with severe *C. striatum* pneumonia, except those reporting hospital outbreak events.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of severe hospital-acquired pneumonia (HAP), and the clinical characteristics and outcomes of severe MRSA pneumonia are well-documented. Therefore, comparing *C. striatum* and MRSA pneumonia could clarify the clinical characteristics of *C. striatum* pneumonia for clinicians. We investigated the proportion, clinical characteristics, and outcomes of severe *C. striatum* pneumonia in adults and compared those aspects with those for severe MRSA pneumonia.

Methods

Study Design, Setting, Data Collection, and Patient Selection

This study is part of an ongoing prospective observational study on severe pneumonia in critically ill adult (≥ 16 years of age) patients at Asan Medical Center, a 2,700-bed tertiary referral center in Seoul, South Korea. Since March 2010, we have prospectively identified all adult patients admitted to the 28-bed medical intensive care unit (ICU) who were clinically suspected of having severe pneumonia and monitored them until hospital discharge (7–10). We collected data on patient demographics; underlying diseases or conditions; category of pneumonia; initial clinical manifestations; laboratory, microbiologic, and radiologic findings; treatment; complications; and mortality rates. For this study, we investigated patients with severe *C. striatum* pneumonia who were admitted to the medical ICU during January 2014–December 2019. This study was approved by the institutional review board of Asan Medical Center (IRB no. 2010–0079), which waived the need for informed consent due to the observational nature of the study.

Definitions

We defined and categorized pneumonia as previously stated (11–13). We defined severe pneumonia as the necessity for mechanical ventilation or having septic shock at ICU admission (12). We defined sepsis and septic shock according to Sepsis-3 criteria (14). We defined immunocompromised state as described previously (15).

C. striatum Identification and Antimicrobial Susceptibility Testing

We cultured sputum specimens on a 5% sheep blood plate and MacConkey agar (Synergy Innovation, <http://www.synergyinno.com>). When coryneform gram-positive bacilli were isolated, we identified and performed antimicrobial susceptibility testing for specimens that were urea positive or from the ICU (16). We quantitatively cultured bronchoalveolar lavage specimens on chocolate agar and identified and performed susceptibility testing when coryneform gram-positive bacilli exclusively grew at $\geq 10^4$ CFU/mL (16). Until August 2015, our facility used the triple sugar iron, motility, API Coryne (bioMérieux-Vitek, <https://www.biomerieux.com>) system to identify coryneform gram-positive rods. In September 2015, our facility began using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonik, <https://www.bruker.com>).

com). We determined antimicrobial susceptibility profiles by ETEST (bioMérieux-Vitek) with MHF medium (Mueller-Hinton agar with 5% horse blood + 20 mg/L β -NAD; bioMérieux-Vitek). We used the Clinical and Laboratory Standards Institute M45 guideline for interpreting susceptibility test results (17) and defined multidrug resistance as resistance to ≥ 3 antimicrobial drug families.

Statistical Analysis

We compared patient demographics, underlying diseases and conditions, and clinical and laboratory parameters between the *C. striatum* group and the MRSA group. We used χ^2 or Fisher exact test to compare categorical variables and Student *t*-test or Mann-Whitney U test to compare continuous variables. We analyzed changes in the proportions of pneumonic pathogens over time by using a χ^2 test for trend. We performed all analyses in SPSS Statistics 24.0 (IBM Corp., <https://www.ibm.com>) and considered $p < 0.05$ statistically significant.

Results

Demographics, Underlying Diseases and Conditions, and Pneumonia Categories

During the study period, we identified a total of 1,740 patients with severe pneumonia. Among them, 27 had severe *C. striatum* pneumonia and 103 had severe MRSA pneumonia (Table 1). The median patient age in the *C. striatum* group was 72.0 years and in the MRSA group was 71.0 years. Solid cancer, diabetes mellitus, and structural lung diseases were the most common underlying conditions in both groups. More patients in the *C. striatum* group were immunocompromised (51.9% vs. 26.2%; $p = 0.01$). Most (70.4%) patients in the *C. striatum* group had HAP, 14.8% had healthcare-associated pneumonia (HCAP), 11.1% had ventilator-associated pneumonia, and 3.7% had CAP. HAP was significantly more common in the *C. striatum* group than the MRSA group (70.4% vs. 42.7%; $p = 0.01$); HCAP was more common in the MRSA group (32.0% vs. 14.8%; $p = 0.08$), albeit without statistical significance.

Table 1. Characteristics of adult patients with severe pneumonia caused by *Corynebacterium striatum*, Seoul, South Korea, 2014–2019*

Characteristics	Total, n = 130	<i>C. striatum</i> , n = 27	MRSA, n = 103	p value
Sex				
M	92 (70.8)	18 (66.7)	74 (71.8)	0.60
F	38 (29.2)	9 (33.3)	33 (32.0)	
Median age (interquartile range)	71.0 (63.8–77.0)	72.0 (66.0–80.0)	71.0 (63.0–76.0)	0.17
Underlying disease or condition†				
Solid cancer	32 (24.6)	4 (14.8)	28 (27.2)	0.18
Diabetes mellitus	30 (23.1)	6 (22.2)	24 (23.3)	0.91
Structural lung disease	24 (18.5)	4 (14.8)	20 (19.4)	0.78
Chronic obstructive lung disease	12 (9.2)	3 (11.1)	9 (8.7)	0.71
Interstitial lung disease	5 (3.8)	0	5 (4.9)	0.58
Bronchiectasis	4 (3.1)	0	4 (3.9)	0.58
Destroyed lung due to tuberculosis	1 (0.8)	0	1 (1.0)	1.00
Pneumoconiosis	1 (0.8)	0	1 (1.0)	1.00
Bronchiolitis obliterans	1 (0.8)	1 (3.7)	0	0.21
Hematologic malignancy	13 (10.0)	5 (18.5)	8 (7.8)	0.14
Liver cirrhosis	11 (8.5)	2 (7.4)	9 (8.7)	1.00
End-stage renal disease	7 (5.4)	2 (7.4)	5 (4.9)	0.64
Chronic renal failure	6 (4.6)	3 (11.1)	3 (2.9)	0.10
Congestive heart failure	3 (2.3)	1 (3.7)	2 (1.9)	0.51
Alcoholism	2 (1.5)	0	2 (1.9)	1.00
Cerebrovascular attack	12 (9.2)	5 (18.5)	7 (6.8)	0.13
Solid organ transplantation	2 (1.5)	0	2 (1.9)	0.63
Hematopoietic stem cell transplantation	3 (2.3)	2 (7.4)	1 (1.0)	0.11
Immunocompromised state‡	41 (31.5)	14 (51.9)	27 (26.2)	0.01
Recent chemotherapy	23 (17.7)	7 (25.9)	16 (15.5)	0.26
Recent surgery, ≤ 1 mo	19 (14.6)	2 (7.4)	17 (16.5)	0.36
Active smoker	10 (7.7)	1 (3.7)	9 (8.7)	0.69
Neutropenia, < 500 cells/mL	8 (6.2)	4 (14.8)	4 (3.9)	0.06
Category of pneumonia				
Community-acquired	6 (4.6)	1 (3.7)	5 (4.9)	1.00
Healthcare-associated	37 (28.5)	4 (14.8)	33 (32.0)	0.08
Hospital-acquired	63 (48.5)	19 (70.4)	44 (42.7)	0.01
Ventilator-associated	24 (18.5)	3 (11.1)	21 (20.4)	0.40

*Values are no. (%) except as indicated. MRSA, methicillin-resistant *Staphylococcus aureus*.

†Patients could have ≥ 1 underlying disease or condition.

‡Defined as ≥ 1 of the following conditions: daily receipt of immunosuppressants, including corticosteroids; HIV infection; solid organ or hematopoietic stem cell transplant recipient; receipt of chemotherapy for underlying malignancy during the previous 6 months; or underlying immune deficiency disorder.

Bacterial Pathogens Identified in Severe HAP Patients

We identified bacterial pathogens in 565 patients who had severe HAP during 2014–2019 (Table 2). The proportion of severe MRSA HAP decreased significantly, from 12.0% (24/200) in 2014–2015 to 2.7% (5/185) in 2018–2019 ($p < 0.01$), whereas the proportion of severe *C. striatum* HAP increased significantly, from 1.0% (2/200) in 2014–2015 to 5.4% (10/185) in 2018–2019 ($p < 0.001$). Among 75 HAP cases from which bacterial pathogens were identified in 2018–2019, *C. striatum* was responsible for 13.3% (10/75) of cases, which was the fourth most common pathogen, after *Acinetobacter baumannii* (30.7%), *Klebsiella pneumoniae* (21.3%), and *Pseudomonas aeruginosa* (14.7%).

Co-infections

We identified co-infection pathogens in 13 (48.1%) patients in the *C. striatum* group and 37 (35.9%) patients in the MRSA group ($p = 0.25$) (Table 3). Co-infection with other bacteria was more common in the MRSA group (25.2% vs. 7.4%; $p = 0.045$), whereas viral co-infection was more common in the *C. striatum* group (33.3% vs. 14.6%; $p = 0.047$). Fungal co-infection, which included 4 *Aspergillus* species and 1 *Pneumocystis jirovecii*, was only found in the *C. striatum* group (14.8% vs. 0%; $p < 0.01$).

Clinical Manifestations and Laboratory Findings

Dyspnea, fever, sputum, and cough were the most common signs and symptoms in both groups (Table 4). Fever tended to be less common in the *C. striatum* group (66.7% vs. 82.5%; $p = 0.07$). The proportion of patients with septic shock at the time of ICU admission was significantly higher in the MRSA group (67.0% vs. 44.4%; $p = 0.03$). However, the proportion of mechanical ventilation, acute physiology and chronic health evaluation (APACHE II) score, and sequential organ failure assessment (SOFA) score at the time of ICU admission were similar between the 2 groups. Peripheral leukocyte counts, platelet counts, and serum C-reactive protein levels also were similar between the 2 groups, but serum procalcitonin level was significantly higher in the MRSA group than the *C. striatum* group (median 0.3 ng/mL vs. 1.8 ng/mL; $p < 0.01$).

C. striatum Gram Stain, Culture, and Antimicrobial Susceptibility Testing

On microscopic examination of Gram stain specimens, gram-positive rods were identified in 69.2% (18/26) of specimens. Among 27 cases, 10 were quantitative cultures and 17 were semiquantitative cultures. Bacterial counts were $>10^5$ CFU/mL in 8/10 quantitative cultures. Of the 17 semiquantitative culture specimens, 12 specimens were grade many (4+), 1 was

Table 2. Bacterial pathogens detected among 565 adult patients with severe hospital-acquired pneumonia, Seoul, South Korea, 2014–2019

Pathogens identified	No. (%) patients				p value*
	2014–2015, n = 200	2016–2017, n = 180	2018–2019, n = 185	Total, n = 565	
Total	88 (44.0)	66 (36.7)	75 (40.5)	229 (40.5)	0.35
<i>Staphylococcus aureus</i>	27 (13.5)	15 (8.3)	8 (4.3)	50 (8.8)	<0.01
Methicillin-susceptible	3 (1.5)	0	3 (1.6)	6 (1.1)	0.24
Methicillin-resistant	24 (12.0)	15 (8.3)	5 (2.7)	44 (7.8)	<0.01
<i>Corynebacterium striatum</i>	2 (1.0)	7 (3.9)	10 (5.4)	19 (3.4)	0.05
<i>Streptococcus pneumoniae</i>	4 (2.0)	2 (1.1)	1 (0.5)	7 (1.2)	0.43
<i>Legionella pneumophila</i>	1 (0.5)	1 (0.6)	0	2 (0.4)	0.61
<i>Moraxella catarrhalis</i>	0	0	1 (0.5)	1 (0.2)	0.36
<i>Streptococcus pyogenes</i>	0	1 (0.6)	0	1 (0.2)	0.34
<i>Nocardia</i> species	0	0	1 (0.5)	1 (0.2)	0.36
Enteric gram-negative bacilli	18 (9.0)	22 (12.2)	20 (10.8)	60 (10.6)	0.59
<i>Klebsiella pneumoniae</i>	13 (6.5)	14 (7.8)	16 (8.6)	43 (7.6)	0.73
<i>Escherichia coli</i>	4 (2.0)	4 (2.2)	3 (1.6)	11 (1.9)	0.92
<i>Enterobacter cloacae</i>	1 (0.5)	3 (1.7)	2 (1.1)	6 (1.1)	0.54
<i>Citrobacter freundii</i>	1 (0.5)	2 (1.1)	0	3 (0.5)	0.34
<i>Klebsiella oxytoca</i>	0	0	2 (1.1)	2 (0.4)	0.13
<i>Hafnia alvei</i>	0	0	1 (0.5)	1 (0.2)	0.36
Nonenteric gram-negative bacilli	47 (23.5)	22 (12.2)	37 (20.0)	106 (18.8)	0.02
<i>Acinetobacter baumannii</i>	24 (12.0)	13 (7.2)	23 (12.4)	60 (10.6)	0.20
<i>Pseudomonas aeruginosa</i>	19 (9.5)	6 (3.3)	11 (5.9)	36 (6.4)	0.047
<i>Stenotrophomonas maltophilia</i>	4 (2.0)	2 (1.1)	7 (3.8)	13 (2.3)	0.22
<i>Burkholderia cepacia</i>	0	0	1 (0.5)	1 (0.2)	0.36
<i>Acinetobacter lwoffii</i>	0	1 (0.6)	0	1 (0.2)	0.34
<i>Chryseobacterium indologenes</i>	0	1 (0.6)	0	1 (0.2)	0.34
<i>Chryseobacterium meningosepticum</i>	1 (0.5)	0	0	1 (0.2)	0.40
<i>Chlamydia pneumoniae</i>	1 (0.5)	0	0	1 (0.2)	0.40

*p value based on χ^2 test for trend.

Table 3. Additional pathogens detected among adult patients with severe *Corynebacterium striatum* pneumonia and methicillin-resistant *Staphylococcus aureus* pneumonia, Seoul, South Korea, 2014–2019*

Pathogens	No. (%) co-infecting pathogens			p value
	Total, n = 130	<i>C. striatum</i> , n = 27	MRSA, n = 103	
Any	50 (38.5)	13 (48.1)	37 (35.9)	0.25
Other bacteria	28 (21.5)	2 (7.4)	26 (25.2)†	0.045
<i>Pseudomonas aeruginosa</i>	7	0	7	
<i>Acinetobacter baumannii</i>	6	0	6	
<i>Klebsiella pneumoniae</i>	5	0	5	
<i>Escherichia coli</i>	4	1	3	
<i>Haemophilus influenzae</i>	2	0	2	
<i>Streptococcus pneumoniae</i>	2	0	2	
<i>Citrobacter freundii</i>	1	0	1	
<i>Enterobacter cloacae</i>	1	1	0	
<i>Elizabethkingia meningosepticum</i>	1	0	1	
<i>Klebsiella aerogenes</i>	1	0	1	
<i>Stenotrophomonas maltophilia</i>	1	0	1	
Virus	24 (18.5)	9 (33.3)‡	15 (14.6)§	0.047
Influenza virus	8	4	4	
Influenza virus A	3	3	0	
Influenza virus B	1	1	1	
Parainfluenza virus type 3	4	1	3	
Rhinovirus	3	1	2	
Adenovirus	3	1	2	
Respiratory syncytial virus	2	1	1	
Respiratory syncytial virus A	1	1	0	
Respiratory syncytial virus B	1	0	1	
Human coronavirus	2	1	1	
229E	1	1	0	
OC43/HKU1	1	0	1	
Human metapneumovirus	2	1	1	
Bocavirus	1	0	1	
Enterovirus	1	0	1	
Fungus	4 (3.1)	4 (14.8)¶	0	<0.01
<i>Aspergillus</i> species	4 (3.1)	4 (14.8)	0	
<i>Pneumocystis jirovecii</i>	1 (0.8)	1 (3.7)	0	

*Categories of co-infection were not mutually exclusive; some cases were associated with ≥2 categories of pathogens.

†Three patients were co-infected with 2 bacteria: *H. influenzae* and *S. pneumoniae*; *E. coli* and *K. pneumoniae*; and *A. baumannii* and *K. pneumoniae*.

‡One patient was co-infected with influenza A virus and human metapneumovirus.

§One patient was co-infected with bocavirus and rhinovirus.

¶One patient was co-infected with *Aspergillus* species and *P. jirovecii*.

grade moderate (3+), 1 grade few (2+), and 3 were grade rare (1+) (Appendix Table, <https://wwwnc.cdc.gov/EID/article/28/11/22-0273-App1.pdf>). All 27 *C. striatum* isolates underwent antimicrobial susceptibility testing. All isolates were resistant to penicillin, ceftriaxone, erythromycin, and ciprofloxacin, and susceptible to vancomycin, and all isolates were multidrug resistant.

Outcomes

The mortality rates between the *C. striatum* and MRSA group showed no statistically significant differences: 30-day mortality (40.7% vs. 29.1%; $p = 0.25$), 60-day (48.1% vs. 42.7%; $p = 0.61$), and 90-day (59.3% vs. 50.5%; $p = 0.42$) (Table 5). In-hospital mortality rates were higher (70.4%) in the *C. striatum* group than in the MRSA group (52.4%), albeit without statistical significance ($p = 0.09$). Mortality rates were similar for *C. striatum* and MRSA in subgroups regardless of the patient's immune status. We noted no statistically significant differences in the median length of ICU

stay between the *C. striatum* and MRSA group, both 14 days ($p = 0.33$), nor in the length of hospital stay after ICU admission, 30 days for the *C. striatum* versus 29 days for the MRSA group ($p = 0.48$).

Discussion

We investigated the proportion and characteristics of severe *C. striatum* pneumonia compared with severe MRSA pneumonia. Although the proportion of severe MRSA HAP greatly decreased during 2014–2019, the proportion of severe *C. striatum* pneumonia sharply increased and surpassed that of severe MRSA pneumonia. *C. striatum* pneumonia was more commonly associated with immunocompromise, viral co-infection, and fungal co-infection. Mortality rates between the *C. striatum* and MRSA groups were comparable.

We found that the proportion of severe MRSA pneumonia decreased while severe *C. striatum* pneumonia greatly increased and that *C. striatum* emerged as one of the most common pathogens in patients with severe HAP. Strengthened infection control measures

SYNOPSIS

Table 4. Clinical and laboratory characteristics of patients with severe *Corynebacterium striatum* pneumonia and methicillin-resistant *Staphylococcus aureus* pneumonia, Seoul, South Korea, 2014–2019*

Characteristics	Total, n = 130	<i>C. striatum</i> , n = 27	MRSA, n = 103	p value
Clinical manifestation				
Dyspnea	106 (81.5)	25 (92.6)	81 (78.6)	0.16
Fever, temperature >38°C	103 (79.2)	18 (66.7)	85 (82.5)	0.07
Sputum	92 (70.8)	16 (59.3)	76 (73.8)	0.14
Cough	57 (43.8)	11 (40.7)	46 (44.7)	0.72
Altered mental status	46 (35.4)	10 (37.0)	36 (35.0)	0.84
Diarrhea	4 (3.1)	2 (7.4)	2 (1.9)	0.19
Septic shock at ICU admission	81 (62.3)	12 (44.4)	69 (67.0)	0.03
Mechanical ventilation	127 (97.7)	27 (100)	100 (97.1)	1.00
APACHE II score, mean (SD)	25.6 (8.1)	26.4 (11.9)	26.0 (7.0)	0.72
SOFA score, mean (SD)	9.5 (3.7)	9.5 (3.4)	9.5 (3.7)	0.99
Bacteremia	19 (14.6)	1 (3.7)	18 (17.5)	0.12
Laboratory findings, median (IQR)				
Leukocyte count, cells/mL	10,950 (7,800–15,625)	11,600 (4,800–15,900)	10,700 (8,400–15,600)	0.26
Platelets, × 10 ³ /mL	159 (81–242)	123 (55–230)	171 (102–245)	0.14
C-reactive protein, mg/dL	11.3 (5.5–19.3)	13.6 (8.0–19.8)	10.8 (5.4–18.6)	0.61
Procalcitonin, ng/mL	1.1 (0.3–3.9)	0.3 (0.1–1.3)	1.8 (0.4–4.2)	<0.01

*Values are no. (%) except as indicated APACHE, acute physiology and chronic health evaluation; BAL, bronchoalveolar lavage; ICU, intensive care unit; IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*; SOFA, sequential organ failure assessment.

during the study period might have contributed to the decline of severe MRSA pneumonia (18); however, severe *C. striatum* pneumonia demonstrated the opposite trend. Several possible explanations for this discrepancy exist. First, detection of *C. striatum* from respiratory specimens in clinical laboratories increased, possibly because experience among laboratory staff accumulated over time. Also, new reliable identification techniques, such as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, were introduced and enabled precise and rapid detection and identification of bacteria in clinical samples, which might have contributed to the increased reports of severe *C. striatum* pneumonia (19,20). Second, *C. striatum* can be resistant to infection control measures and can adhere to abiotic surfaces and form biofilms on various

medical devices, such as feeding tubes, endotracheal tubes, and ventilators (21,22). Some reports documented *C. striatum* strains with resistance to high-level disinfectants, such as 2% glutaraldehyde and other biocides (23,24). These findings suggest that appropriate environmental infection control measures for *C. striatum* should be further investigated and implemented. Finally, hospital outbreaks also might have contributed to the seeming discrepancy. Colonized patients and contaminated inanimate objects could be reservoirs for prolonged outbreaks. However, when we chronologically analyzed the occurrence patterns according to time and place, we could not find any suggestions of notable outbreaks. Clinical observation alone creates difficulties and limitations in distinguishing outbreaks; therefore, future studies should include more detailed

Table 5. Outcomes of adult patients with severe *Corynebacterium striatum* and methicillin-resistant *Staphylococcus aureus* pneumonia, Seoul, South Korea, 2014–2019*

Outcome	Total, n = 130	<i>C. striatum</i> , n = 27	MRSA, n = 103	p value
Death				
Total	n = 103	n = 27	n = 103	NA
30 days	41 (31.5)	11 (40.7)	30 (29.1)	0.25
60 days	57 (43.8)	14 (48.1)	44 (42.7)	0.61
90 days	68 (52.3)	16 (59.3)	52 (50.5)	0.42
In-hospital	73 (56.2)	19 (70.4)	54 (52.4)	0.09
Death among patient categories				
Nonimmunocompromised patients	n = 89	n = 13	n = 76	NA
30 days	21 (23.6)	5 (38.5)	16 (21.1)	0.18
60 days	31 (34.8)	5 (38.5)	26 (34.2)	0.76
90 days	40 (44.9)	7 (53.8)	33 (43.4)	0.49
In-hospital	40 (44.9)	7 (53.8)	33 (43.4)	0.49
Immunocompromised patients	n = 41	n = 14	n = 27	NA
30 days	20 (48.8)	6 (42.9)	14 (51.9)	0.59
60 days	26 (63.4)	8 (57.1)	18 (66.7)	0.55
90 days	28 (68.3)	9 (64.3)	19 (70.4)	0.73
In-hospital	33 (80.5)	12 (85.7)	21 (77.8)	0.69
Median ICU stay, d (IQR)	14.0 (8.0–26.3)	14.0 (9.0–27.0)	14.0 (8.0–26.0)	0.33
Median hospital stay after ICU admission, d (IQR)	29.5 (14.0–57.0)	30.0 (16.0–81.0)	29.0 (14.0–55.0)	0.48

*Values are no. (%) except as indicated. ICU, intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*; NA, not applicable.

typing analysis of *C. striatum* isolates to identify and curb possible healthcare-associated outbreaks.

In this study, viral or fungal co-infection was more common in the *C. striatum* group, whereas other bacterial co-infection was more common in the MRSA group. This finding could represent the host factor because a greater proportion of *C. striatum* patients were in an immunocompromised state, which would make them vulnerable to opportunistic infections. Of note, fewer cases of bacterial coinfection were diagnosed in the *C. striatum* group, but the cause for this difference is uncertain. One possible explanation is that *C. striatum* might influence the behavior and fitness of other bacteria. A recent study reported that *Corynebacterium* species can reduce the toxicity of *Staphylococcus aureus* by exhibiting decreased hemolysin activity and displaying diminished fitness of in vivo coinfection (25). Further targeted studies on this issue are needed.

We found that serum procalcitonin level was higher in the MRSA group than in the *C. striatum* group (median 1.8 ng/mL vs. 0.3 ng/mL). Some studies suggest that serum procalcitonin can be used as a marker for bacterial infection and to differentiate bacterial from viral infection or noninfectious causes of inflammation (26,27). In 2017, a group of researchers in China reported that the median serum procalcitonin level of an *S. aureus* bacteremia group of patients was higher (1.18 ng/mL) than that of a coagulase-negative staphylococci bacteremia group (0.21–0.31 ng/mL) (28). We speculate that infections caused by low-virulence bacteria, such as *C. striatum* in our study, might have low levels of procalcitonin and this warrants further investigation.

Mortality rates were similarly high in both groups, but septic shock at the time of initial clinical manifestation was less common in the *C. striatum* group. Immunocompromised conditions were more common in the *C. striatum* group, which could suggest that *C. striatum* is less virulent than MRSA. Host factor might contribute to the development of severe *C. striatum*-associated pneumonia and the subsequent outcomes; however, we noted no statistically significant differences in mortality rates between the 2 groups after stratification by immunocompromised conditions. The existence of co-infection and pathogen types (e.g., other bacteria, viruses, fungi) involved might have affected mortality rates, but we were unable to effectively evaluate each effect because of the small number of patients in each subgroup.

The first limitation of our study is that we used a single-center design and our results might not be replicable in other centers or hospital systems. In addition, as we mentioned previously, we were not able to effectively evaluate the sole contribution of

C. striatum because co-infection with other pathogens was common among the patient cohort. Finally, we included all *C. striatum* isolates from sputum, endotracheal aspirate, and bronchoalveolar lavage, but the cultures were mostly semiquantitative, and some of the *C. striatum* isolates might have been nonpathogenic colonizers. A 2020 study from the United States reported that normal respiratory flora appears to have caused one quarter of CAP cases (29), which supports our finding that bacteria previously considered as colonizers or normal flora can be a cause of pneumonia.

In conclusion, we found *C. striatum* was associated with severe HAP. Patients with severe *C. striatum* pneumonia showed similar clinical and laboratory features as patients with severe MRSA pneumonia, and both infections were associated with high mortality rates. Further investigations could clarify incidence, clinical characteristics, and outcomes of severe *C. striatum* pneumonia in critically ill adults and determine whether infections are due to colonization, or community- or healthcare-acquired infections. Clinicians should be aware of this emerging pathogen as a possible cause for severe pneumonia, especially among immunocompromised patients.

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References

1. Funke G, von Graevenitz A, Clarridge JE III, Bernard KA. Clinical microbiology of coryneform bacteria. *Clin Microbiol Rev.* 1997;10:125–59. <https://doi.org/10.1128/CMR.10.1.125>
2. Chen FL, Hsueh PR, Teng SO, Ou TY, Lee WS. *Corynebacterium striatum* bacteremia associated with central venous catheter infection. *J Microbiol Immunol Infect.* 2012;45:255–8. <https://doi.org/10.1016/j.jmii.2011.09.016>
3. Hong HL, Koh HI, Lee AJ. Native valve endocarditis due to *Corynebacterium striatum* confirmed by 16S ribosomal RNA sequencing: a case report and literature review. *Infect Chemother.* 2016;48:239–45. <https://doi.org/10.3947/ic.2016.48.3.239>
4. Bowstead TT, Santiago SM Jr. Pleuropulmonary infection due to *Corynebacterium striatum*. *Br J Dis Chest.* 1980;74:198–200. [https://doi.org/10.1016/0007-0971\(80\)90035-2](https://doi.org/10.1016/0007-0971(80)90035-2)

5. Díez-Aguilar M, Ruiz-Garbjosa P, Fernández-Olmos A, Guisado P, Del Campo R, Quereda C, et al. Non-diphtheriae *Corynebacterium* species: an emerging respiratory pathogen. *Eur J Clin Microbiol Infect Dis*. 2013;32:769–72. <https://doi.org/10.1007/s10096-012-1805-5>
6. Yang K, Kruse RL, Lin WV, Musher DM. *Corynebacteria* as a cause of pulmonary infection: a case series and literature review. *Pneumonia (Nathan)*. 2018;10:10. <https://doi.org/10.1186/s41479-018-0054-5>
7. Choi SH, Hong SB, Ko GB, Lee Y, Park HJ, Park SY, et al. Viral infection in patients with severe pneumonia requiring intensive care unit admission. *Am J Respir Crit Care Med*. 2012;186:325–32. <https://doi.org/10.1164/rccm.201112-2240OC>
8. Hong HL, Hong SB, Ko GB, Huh JW, Sung H, Do KH, et al. Viral infection is not uncommon in adult patients with severe hospital-acquired pneumonia. *PLoS One*. 2014;9:e95865. <https://doi.org/10.1371/journal.pone.0095865>
9. Choi SH, Hong SB, Hong HL, Kim SH, Huh JW, Sung H, et al. Usefulness of cellular analysis of bronchoalveolar lavage fluid for predicting the etiology of pneumonia in critically ill patients. *PLoS One*. 2014;9:e97346. <https://doi.org/10.1371/journal.pone.0097346>
10. Choi SH, Huh JW, Hong SB, Lee JY, Kim SH, Sung H, et al. Clinical characteristics and outcomes of severe rhinovirus-associated pneumonia identified by bronchoscopic bronchoalveolar lavage in adults: comparison with severe influenza virus-associated pneumonia. *J Clin Virol*. 2015;62:41–7. <https://doi.org/10.1016/j.jcv.2014.11.010>
11. American Thoracic Society/Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2005;171:388–416. <https://doi.org/10.1164/rccm.200405-644ST>
12. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al.; Infectious Diseases Society of America; American Thoracic Society. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007;44:S27–72. <https://doi.org/10.1086/511159>
13. Carratalà J, Mykietiak A, Fernández-Sabé N, Suárez C, Dorca J, Verdager R, et al. Health care-associated pneumonia requiring hospital admission: epidemiology, antibiotic therapy, and clinical outcomes. *Arch Intern Med*. 2007;167:1393–9. <https://doi.org/10.1001/archinte.167.13.1393>
14. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315:801–10. <https://doi.org/10.1001/jama.2016.0287>
15. Micek ST, Kollef KE, Reichley RM, Roubinian N, Kollef MH. Health care-associated pneumonia and community-acquired pneumonia: a single-center experience. *Antimicrob Agents Chemother*. 2007;51:3568–73. <https://doi.org/10.1128/AAC.00851-07>
16. Gilligan PH, Alby K, York MK. Respiratory tract cultures. In: Leber AL, editor. *Clinical microbiology procedures handbook*, 4th edition, volume 1. Washington: ASM Press; 2016. pp. 3.11.1.1–9.4.
17. Clinical and Laboratory Standards Institute. *Methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria*, third edition (M45). Wayne (PA): The Institute; 2016.
18. Kim H, Kim ES, Lee SC, Yang E, Kim HS, Sung H, et al. Decreased incidence of methicillin-resistant *Staphylococcus aureus* bacteremia in intensive care units: a 10-year clinical, microbiological, and genotypic analysis in a tertiary hospital. *Antimicrob Agents Chemother*. 2020;64:e01082-20. <https://doi.org/10.1128/AAC.01082-20>
19. Khamis A, Raoult D, La Scola B. Comparison between *rpoB* and 16S rRNA gene sequencing for molecular identification of 168 clinical isolates of *Corynebacterium*. *J Clin Microbiol*. 2005;43:1934–6. <https://doi.org/10.1128/JCM.43.4.1934-1936.2005>
20. Vila J, Juiz P, Salas C, Almela M, de la Fuente CG, Zboromyrska Y, et al. Identification of clinically relevant *Corynebacterium* spp., *Arcanobacterium haemolyticum*, and *Rhodococcus equi* by matrix-assisted laser desorption/ionization-time-of-flight mass spectrometry. *J Clin Microbiol*. 2012;50:1745–7. <https://doi.org/10.1128/JCM.05821-11>
21. Souza C, Faria YV, Sant'Anna LO, Viana VG, Seabra SH, Souza MC, et al. Biofilm production by multidrug-resistant *Corynebacterium striatum* associated with nosocomial outbreak. *Mem Inst Oswaldo Cruz*. 2015;110:242–8. <https://doi.org/10.1590/0074-02760140373>
22. Ramos JN, Souza C, Faria YV, da Silva EC, Veras JFC, Baio PVP, et al. Bloodstream and catheter-related infections due to different clones of multidrug-resistant and biofilm producer *Corynebacterium striatum*. *BMC Infect Dis*. 2019;19:672. <https://doi.org/10.1186/s12879-019-4294-7>
23. Souza C, Mota HF, Faria YV, Cabral FO, Oliveira DR, Sant'Anna LO, et al. Resistance to antiseptics and disinfectants of planktonic and biofilm-associated forms of *Corynebacterium striatum*. *Microb Drug Resist*. 2020;26:1546–58. <https://doi.org/10.1089/mdr.2019.0124>
24. Silva-Santana G, Silva CMF, Olivella JGB, Silva IF, Fernandes LMO, Sued-Karam BR, et al. Worldwide survey of *Corynebacterium striatum* increasingly associated with human invasive infections, nosocomial outbreak, and antimicrobial multidrug-resistance, 1976–2020. *Arch Microbiol*. 2021;203:1863–80. <https://doi.org/10.1007/s00203-021-02246-1>
25. Ramsey MM, Freire MO, Gabriliska RA, Rumbaugh KP, Lemon KP. *Staphylococcus aureus* shifts toward commensalism in response to *Corynebacterium* species. *Front Microbiol*. 2016;7:1230. <https://doi.org/10.3389/fmicb.2016.01230>
26. Simon L, Gauvin F, Amre DK, Saint-Louis P, Lacroix J. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. *Clin Infect Dis*. 2004;39:206–17. <https://doi.org/10.1086/421997>
27. Limper M, de Kruif MD, Duits AJ, Brandjes DP, van Gorp EC. The diagnostic role of procalcitonin and other biomarkers in discriminating infectious from non-infectious fever. *J Infect*. 2010;60:409–16. <https://doi.org/10.1016/j.jinf.2010.03.016>
28. Yan ST, Sun LC, Jia HB, Gao W, Yang JP, Zhang GQ. Procalcitonin levels in bloodstream infections caused by different sources and species of bacteria. *Am J Emerg Med*. 2017;35:579–83. <https://doi.org/10.1016/j.ajem.2016.12.017>
29. Musher DM, Jesudasan SS, Barwatt JW, Cohen DN, Moss BJ, Rodriguez-Barradas MC. Normal respiratory flora as a cause of community-acquired pneumonia. *Open Forum Infect Dis*. 2020;7:ofaa307. <https://doi.org/10.1093/ofid/ofaa307>

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