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### ***Corynebacterium striatum* in the Respiratory Tract of Intensive Care Unit Patients: Pathogen or Colonizer? A Decade-Long Retrospective Study**

**Nadir et al. *Corynebacterium striatum*, Pathogen or Colonizer?**

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#### **Abstract**

**Introduction:** *Corynebacterium striatum* has emerged as a significant nosocomial pathogen, particularly among intensive care unit (ICU) patients. This study aimed to determine whether *Corynebacterium striatum* isolated from respiratory samples represents true infection or colonization and to identify risk factors distinguishing these conditions.

**Materials and Methods:** We conducted a retrospective cohort study from June 2015 to June 2025, including adult ICU patients with *Corynebacterium striatum* isolated from respiratory specimens. Patients were classified into pneumonia or colonization/contamination (CC) groups. Risk factors were analyzed using descriptive statistics, univariate comparisons, and multivariate binary logistic regression to identify independent predictors of pneumonia.

**Results:** Among 396 patients, 126 (31.8%) were classified in the pneumonia group and 270 (68.2%) in the CC group. Chronic obstructive pulmonary disease (COPD; 31% vs. 2.2%,  $p < 0.001$ ) and cardiovascular disease (22.2% vs. 11.5%,  $p = 0.005$ ) were more prevalent in the pneumonia group. Multivariate analysis identified COPD (adjusted odds ratio [OR] = 26.67; 95% confidence interval [CI] = 5.05–140.91;  $p < 0.001$ ) and Bartlett score (adjusted OR = 20.61; 95% CI = 10.99–38.61;  $p < 0.001$ ) as independent predictors of pneumonia. The area under the receiver operating characteristic curve for the Bartlett score was 0.941 (95% CI = 0.914–0.968); a score  $\geq 1$  had 92% sensitivity and 93% specificity for predicting pneumonia.

**Conclusion:** Isolation of *Corynebacterium striatum* from respiratory samples in ICU patients should not be automatically dismissed as contamination, particularly in patients with COPD or specimens with higher Bartlett scores. Assessment of specimen quality provides valuable diagnostic insight, and ongoing surveillance of antimicrobial resistance remains essential.

**Key words:** Colonization, *Corynebacterium striatum*, intensive care unit, pneumonia

#### **Introduction**

*Corynebacterium striatum*, formerly considered a harmless skin commensal, has recently emerged as a significant opportunistic pathogen, particularly in healthcare settings. It is increasingly isolated from clinical specimens, especially in patients with prolonged hospital stays, invasive devices, or prior antibiotic exposure, and has been implicated in various nosocomial infections, including respiratory tract infections (RTIs), bloodstream infections, and surgical site infections<sup>[1-3]</sup>.

In hospitals, particularly among immunocompromised patients, those with chronic pulmonary disease or malignancy, or those undergoing hemodialysis, *Corynebacterium striatum* infections are associated with high morbidity and mortality. Lee et al. reported that *Corynebacterium striatum* isolated from blood cultures was predominantly healthcare-associated and linked to 30-day mortality. In a retrospective cohort of intensive care unit (ICU) patients, *Corynebacterium striatum* was identified as the etiologic agent in a substantial proportion of ventilator-associated pneumonia cases, with outcomes comparable to those caused by *Staphylococcus aureus*<sup>[3,4]</sup>.

Although traditionally underrecognized, the rising frequency and clinical severity of *Corynebacterium striatum* infections underscore the need for heightened awareness and accurate microbiological identification to differentiate colonization from true infection. Modern diagnostic tools, including matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry and genome sequencing, have enhanced detection and epidemiological surveillance of this pathogen<sup>[1-5]</sup>. Recent studies indicate that *Corynebacterium striatum* frequently exhibits resistance to  $\beta$ -lactams, macrolides, aminoglycosides, and fluoroquinolones, while retaining susceptibility primarily to glycopeptides (vancomycin, teicoplanin) and oxazolidinones (linezolid) [6-7].

This study aims to evaluate the clinical significance and risk factors of RTIs caused by *Corynebacterium striatum* in ICU patients and to provide guidance for distinguishing true infections from colonization or contamination.

## Materials and Methods

### Study Design

This retrospective cohort study was conducted at a tertiary research hospital in İzmir, Türkiye, from June 2015 to June 2025. Eligible participants were adult ICU inpatients who met all of the following criteria: (a) ICU admission; (b) isolation of *Corynebacterium striatum* from a respiratory tract culture obtained  $\geq 48$  hours after ICU admission; and (c) age  $\geq 18$  years. Patients were classified into two groups for analysis: colonization/contamination (CC; n = 270) and pneumonia (n = 126).

Sample size calculations were performed using OpenEpi Version 3.01, estimating that 264 patients were required to achieve 80% power with a type I error rate of 5%.

The study was approved by the University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital Ethics Committee for Non-Interventional Research (approval number: 2025/05-24, dated: 12.06.2025). As this was a retrospective observational study using de-identified patient data, written informed consent was waived by the ethics committee.

### Definition of CC and Infection

RTIs were defined according to the Centers for Disease Control and Prevention and European Centre for Disease Prevention and Control criteria for hospital-acquired pneumonia and ventilator-associated pneumonia<sup>[8-9]</sup>. A positive culture from respiratory specimens (tracheal aspirate, bronchoalveolar lavage, or sputum) was considered indicative of infection only if accompanied by compatible clinical findings, including new or progressive pulmonary infiltrates on imaging, fever ( $>38$  °C), leukocytosis or leukopenia, and purulent tracheal secretions.

Colonization or contamination was defined as the isolation of microorganisms from respiratory samples in the absence of clinical, radiological, or laboratory evidence of infection. Repeated isolation of the same organism without clinical deterioration was also considered colonization. Classification of patients as pneumonia or colonization was performed by an infectious diseases specialist during consultation, based solely on CDC criteria and without reference to the Bartlett score during the initial clinical assessment.

### Data Collection

The primary outcome was 30-day mortality. Secondary variables included the antimicrobial resistance profile of *Corynebacterium striatum*, Bartlett scores of respiratory specimens, and concomitant infections. Patient demographics, comorbidities, and other clinical variables were extracted from electronic medical records.

### Microbiological Analysis

Respiratory specimens were evaluated using Gram staining and direct microscopic examination. The quality of all specimens was routinely assessed using the Bartlett scoring system. For this study, Bartlett scores were calculated retrospectively for analytical purposes only and were not used to guide diagnostic classification, minimizing the risk of classification bias. The Bartlett score quantifies polymorphonuclear leukocytes, squamous epithelial cells, and mucus under low-power field microscopy ( $\times 100$ )<sup>[10]</sup>. Scores were assigned as follows:

- Neutrophils per 10 low-power fields (LPFs):  $<10 = 0$ ;  $10-25 = +1$ ;  $>25 = +2$
- Presence of mucus: +1
- Epithelial cells per 10 LPFs:  $10-25 = -1$ ;  $>25 = -2$

The total Bartlett score was obtained by summing these parameters<sup>[10]</sup>.

Following microscopic evaluation, specimens were inoculated onto 5% sheep blood, eosin methylene blue (EMB), and chocolate agar (bioMérieux®, France). Blood and EMB agar plates were incubated aerobically at 35 °C for 24–48 hours, while chocolate agar plates were incubated under 5% CO<sub>2</sub> at 35 °C. Colonies with morphology consistent with *Corynebacterium* species were identified using MALDI-TOF MS (Bruker Daltonics®, Germany). Antimicrobial susceptibility testing was performed using the disk diffusion method on Mueller-Hinton Fastidious agar (bioMérieux®, France) according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. Susceptibility results were interpreted based on the EUCAST breakpoints valid at the time of testing<sup>[11]</sup>. Cases in which additional microorganisms were detected alongside *Corynebacterium striatum* in the same specimen were recorded as concomitant microorganisms.

### Statistical Analysis

Normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Non-normally distributed variables were summarized as median and interquartile range (IQR; Q1-Q3). Categorical variables were presented as counts (n) and percentages (%).

Variables with  $p < 0.10$  in univariate analyses—including age, sex, comorbidities, intubation status, Coronavirus Disease 2019 (COVID-19) status, concomitant microorganisms, and Bartlett score—were included in a multivariate binary logistic regression model to identify independent predictors of pneumonia caused by *Corynebacterium striatum*. Multicollinearity was assessed using variance inflation factors and was not observed. Associations were expressed as adjusted odds ratios (ORs) with 95% confidence intervals (CIs).

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of the Bartlett score in distinguishing true *Corynebacterium striatum* pneumonia from colonization. The area under the curve (AUC) with 95% CI was calculated, and the optimal cutoff value was determined using the Youden index. Statistical significance was defined as  $p < 0.05$ . Analyses were performed using IBM SPSS Statistics, version 26.0.

## Results

A total of 396 patients were included, of whom 126 (31.8%) were classified in the pneumonia group and 270 (68.2%) in the CC group. In the pneumonia group, 120 lower respiratory tract samples (95.2%) and six sputum samples (4.8%) were evaluated, whereas 146 lower respiratory tract samples (85.9%) and 24 sputum samples (14.1%) were observed in the CC group. The proportions of specimen types were similar between the two groups ( $p = 0.214$ ), indicating that subsequent analyses were balanced with respect to specimen type.

Patient characteristics are summarized in Table 1. The median age of patients with pneumonia was 76.5 years (IQR, 64.8–85.3), comparable to the CC group (75 [63.5–83] years;  $p = 0.350$ ). Gender distribution was similar, with males comprising 57.9% of the pneumonia group and 60.7% of the CC group ( $p = 0.596$ ). Among comorbidities, chronic obstructive pulmonary disease (COPD; 31% vs. 2.2%,  $p < 0.001$ ) and cardiovascular disease (22.2% vs. 11.5%,  $p = 0.005$ ) were significantly more frequent in patients with pneumonia. No significant differences were observed for diabetes mellitus, hypertension, or chronic kidney disease. Thirty-day all-cause mortality was significantly higher in the pneumonia group compared with the CC group (43.7% vs. 11.1%;  $p < 0.001$ ).

Among the 396 patients, 328 (82.8%) were intubated at the time of respiratory culture sampling, whereas 68 (17.2%) were not. The rate of tracheal intubation did not differ significantly between the pneumonia and CC groups.

Analysis of the antimicrobial resistance profile of *Corynebacterium striatum* isolates showed the highest resistance to penicillin (41.4%), followed by gentamicin (27.8%), ciprofloxacin (19.2%), and clindamycin (13.4%). Resistance to erythromycin was low (3.3%), and no resistance was detected to vancomycin or linezolid. The resistance patterns were similar between the pneumonia and CC groups, with no statistically significant differences.

The presence of concomitant bacterial microorganisms and the coexistence of COVID-19 infection were evaluated. Both conditions were similarly distributed between the pneumonia and CC groups, with no statistically significant differences. Similarly, immunosuppressive conditions, including cancer, did not differ significantly between groups.

The Bartlett score, reflecting the quality of sputum specimens, was markedly higher in the pneumonia group compared with the CC group. In the binary logistic regression analysis (Table 2), COPD and Bartlett score were identified as independent risk factors for pneumonia caused by *Corynebacterium striatum*. Patients with COPD had a 26.7-fold higher likelihood of developing pneumonia (adjusted OR = 26.67; 95% CI = 5.05–140.91;  $p < 0.001$ ), whereas each one-point increase in Bartlett score was associated with a 20.6-fold increase in the odds of pneumonia (adjusted OR = 20.61; 95% CI = 10.99–38.61;  $p < 0.001$ ). ROC analysis of the Bartlett score yielded an AUC of 0.941 (95% CI = 0.914–0.968; Figure 1). A Bartlett score of  $\geq 1$  demonstrated 92% sensitivity and 93% specificity for predicting pneumonia.

Cancer showed a borderline association with pneumonia (adjusted OR = 3.33; 95% CI = 0.99–11.17;  $p = 0.052$ ), whereas cerebrovascular disease was not significantly associated. The overall model was statistically significant (Omnibus test,  $p < 0.001$ ; -2 Log Likelihood = 165.59) and demonstrated good calibration (Hosmer–Lemeshow test,  $p = 0.135$ ).

## Discussion

*Corynebacterium striatum* is increasingly recognized as a significant cause of nosocomial infections and outbreaks worldwide, affecting both immunocompromised and immunocompetent patients and occasionally leading to severe or fatal invasive disease<sup>[12]</sup>. Experimental studies have shown that *Corynebacterium striatum* induces marked lung inflammation and pathological changes, with a more pronounced inflammatory response observed in immunocompromised mice<sup>[13]</sup>.

The primary objective of this study was to determine whether *Corynebacterium striatum* isolates from respiratory samples of ICU patients represent true infection or colonization and to identify risk factors that differentiate these conditions. By clarifying this distinction, our findings aim to support more accurate clinical decision-making and optimize management strategies for critically ill patients with *Corynebacterium striatum* isolation.

We evaluated 396 ICU patients with respiratory specimens positive for *Corynebacterium striatum*. Age and sex distributions were similar between the pneumonia and CC groups; however, significant differences were observed in comorbidity profiles. COPD and cardiovascular disease were more prevalent in the pneumonia group, with COPD emerging as a strong independent risk factor in multivariate analysis (adjusted OR = 26.67; 95% CI = 5.05–140.91;  $p < 0.001$ ). These findings suggest that *Corynebacterium striatum* may act as a true respiratory pathogen, particularly in patients with underlying structural lung disease. Previous studies similarly reported that *Corynebacterium striatum* infections predominantly occur in individuals with severe COPD or other chronic pulmonary conditions<sup>[13]</sup>. To our knowledge, this study is the first to demonstrate that COPD is not only a predisposing condition but also an independent risk factor for invasive infection caused by *Corynebacterium striatum*.

In our cohort, 30-day all-cause mortality was significantly higher in the pneumonia group than in the CC group (43.7% vs. 11.1%;  $p < 0.001$ ), emphasizing the clinical relevance of *Corynebacterium striatum* pneumonia. This observation aligns with previous reports; a study from South Korea comparing pneumonia caused by *Corynebacterium striatum* and methicillin-resistant *Staphylococcus aureus* found similarly high mortality rates in both groups<sup>[14]</sup>. These findings highlight *Corynebacterium striatum* as an emerging cause of severe pneumonia, particularly among critically ill patients.

In contrast to prior studies, the distribution of immunosuppressed patients was similar between the pneumonia and CC groups in our cohort. This may reflect the high prevalence of underlying comorbidities and overall critical illness among ICU patients, potentially masking the effect of immunosuppression as a differentiating factor. Similarly, endotracheal intubation rates did not differ significantly between groups, likely because the uniformly severe clinical condition of ICU patients limited the discriminatory value of this variable.

In this study, *Corynebacterium striatum* isolates exhibited high resistance rates to penicillin (41.4%), gentamicin (27.8%), ciprofloxacin (19.2%), and clindamycin (13.4%), whereas resistance to erythromycin was low (3.3%), and no resistance was observed for vancomycin or linezolid. These findings are consistent with previous reports indicating that *Corynebacterium striatum* frequently exhibits multidrug resistance while remaining generally susceptible to glycopeptides and oxazolidinones<sup>[15,16]</sup>. The observation that both colonizing and pathogenic isolates shared similar resistance profiles suggests that antimicrobial resistance in *Corynebacterium striatum* is largely driven by environmental selection pressure from sustained antibiotic exposure in hospital settings rather than by intrinsic infection-related properties of the strain. This underscores *Corynebacterium striatum* as a highly

adapted nosocomial colonizer capable of persisting in ICU environments and indicates that antimicrobial resistance alone cannot distinguish true infection from colonization.

Recent studies have reported increased *Corynebacterium striatum* isolation during the COVID-19 pandemic<sup>[17]</sup>. In our cohort, COVID-19 infection was more frequently observed in the pneumonia group, reflecting the known susceptibility of patients with viral pneumonia to secondary bacterial infections and impaired airway defense mechanisms. However, as COVID-19 status did not remain an independent predictor in multivariate analysis, this association should be interpreted cautiously and may serve as a marker of overall disease severity rather than a direct causal factor.

The Bartlett score, reflecting specimen quality, was significantly higher in patients with pneumonia. Each one-point increase was associated with a 20.6-fold increase in the odds of pneumonia. ROC analysis demonstrated excellent discriminative performance of the Bartlett score in distinguishing true *Corynebacterium striatum* pneumonia from colonization or contamination, with an AUC of 0.941 (95% CI = 0.914–0.968). A Bartlett score  $\geq 1$  yielded 92% sensitivity and 93% specificity for predicting pneumonia, suggesting that this threshold may serve as a practical cutoff in clinical settings. These results emphasize that sputum quality assessment is not merely a laboratory procedure but a clinically meaningful parameter that can guide interpretation of *Corynebacterium striatum* isolates.

This study has several limitations. First, it was a retrospective, single-center study, which may limit generalizability. Second, detailed data on prior antibiotic use, duration of mechanical ventilation, severity of illness, and other invasive procedures were incomplete, potentially introducing confounding variables. Third, although the Bartlett score was calculated retrospectively and not used for clinical adjudication, the strong association observed may partly reflect conceptual overlap between specimen quality and the clinical definition of pneumonia, potentially inflating its effect size.

### Conclusion

This study underlines that *Corynebacterium striatum* isolation from respiratory specimens in ICU patients should not be automatically dismissed as contamination, particularly in patients with COPD. The study also highlights the diagnostic value of specimen quality, suggesting that isolates with higher Bartlett scores are more likely to represent true infection rather than colonization.

### Ethics

**Ethics Committee Approval:** The study was approved by the University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital Ethics Committee for Non-Interventional Research (approval number: 2025/05-24, dated: 12.06.2025).

**Informed Consent:** Retrospective study.

### Footnotes

### Authorship Contributions

Concept: Y.N., Design: Y.N., P.K., S.A., Data Collection or Processing: Y.N., M.A.Ö., Analysis or Interpretation: Y.N., P.K., M.A.Ö., S.A., Literature Search: Y.N., S.A., Writing: Y.N.

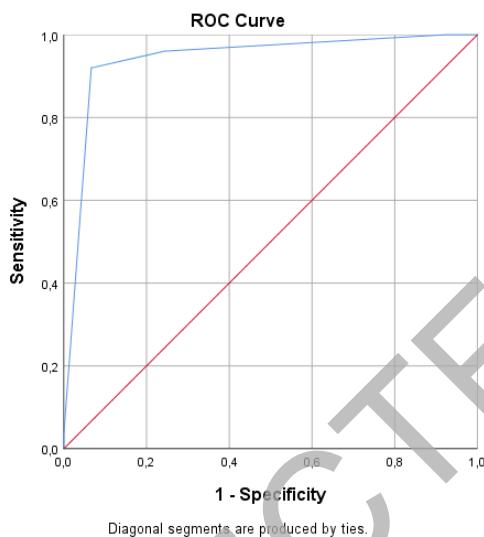
**Conflict of Interest:** No conflict of interest was declared by the author(s).

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**Figure 1.** ROC curve for the diagnosis of pneumonia.

ROC, receiver operating characteristic.

**Table 1.** Characteristics of patients in the pneumonia and CC groups.

	Pneumonia group, (n = 126)	CC group, (n = 270)	p-value
Age, years	76.5 (64.8–85.3)	75 (63.5–83)	0.350
Gender, male	73 (57.9)	164 (60.7)	0.596
<b>Comorbidities</b>			
Diabetes mellitus	50 (39.7)	129 (47.8)	0.133
Hypertension	21 (16.7)	52 (19.3)	0.535
COPD	39 (31)	6 (2.2)	<0.001
Cardiovascular disease	28 (22.2)	31 (11.5)	0.005
Cerebrovascular disease	6 (4.8)	16 (5.9)	0.638
Chronic kidney disease	9 (7.1)	12 (4.4)	0.264
Cancer/immunosuppression	20 (15.9)	24 (8.9)	0.039
Tracheal intubation	110 (87.3)	218 (80.7)	0.107
COVID-19 infection	22 (17.5)	23 (8.5)	0.021
Concomitant microorganisms*	32 (25.4)	82 (30.4)	0.309
Bartlett score	2 (2–2)	0 (0–0)	<0.001
Penicillin resistance	123 (97.6)	258 (95.6)	0.316
30-day mortality: 55 (43.7%) in pneumonia group, 30 (11.1%) in CC group; p < 0.001.			
Data are presented as median (IQR) or n (%). *Concomitant microorganisms: Cases in which additional microorganisms were detected alongside <i>Corynebacterium striatum</i> in the same respiratory sample. CC, colonization/contamination; COPD, chronic obstructive pulmonary disease; COVID-19, Coronavirus Disease 2019; IQR, interquartile range.			

**Table 2.** Risk factors for pneumonia based on binary logistic regression analysis (enter method).

Covariate	Adjusted OR (95% CI)	p-value
COPD	26.67 (5.05–140.91)	<0.001
Cerebrovascular disease	1.98 (0.66–5.95)	0.223
Cancer	3.33 (0.99–11.17)	0.052
Bartlett score	20.61 (10.99–38.61)	<0.001

Omnibus test:  $p < 0.001$ . -2 Log Likelihood: 165.59. Hosmer-Lemeshow test:  $p = 0.135$ . CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio.

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