BMC Infectious Diseases

RESEARCH

Open Access

Comparison of bloodstream infections due to *Corynebacterium striatum*, MRSA, and MRSE

Shu-Hua He[1], Yan Chen[1], Hong-Li Sun[2], Shan Li[1], Shi-Tong Diao[1], Yi-Fan Wang[1], Zhuo-Xin He[1], Li Weng[1], Jin-Min Peng[1*] and Bin Du[1*]

Abstract

Background *Corynebacterium striatum* (*C. striatum*), a common skin and mucosal colonizer, is increasingly considered as an opportunistic pathogen causing bloodstream infections (BSIs). This study aims to investigate the clinical features and outcomes of *C. striatum*-BSI.

Methods We included hospitalized cases with *C. striatum*-positive blood cultures from January 2014 to June 2022 and classified them into *C. striatum*-BSI group and contamination group; Clinical characteristics, treatments, and outcomes were compared between the *C. striatum*-BSI group and contamination group, Methicillin-resistant *Staphylococcus aureus* (MRSA)-BSI and Methicillin-resistant *Staphylococcus epidermidis* (MRSE)-BSI.

Results Fifty-three patients with positive *C. striatum* blood cultures were identified. Among them, 25 patients were classified as *C. striatum*-BSI, with 21 as contamination cases. And 62 cases of MRSA-BSI and 44 cases of MRSE-BSI were identified. Compared to the contaminated group, the *C. striatum*-BSI group had a shorter time to positivity of blood cultures (27.0 h vs. 42.5 h, $P=0.011$). *C. striatum*-BSI group had a longer time to positivity (27 h) when compared to both the MRSA (20 h) and MRSE groups (19 h) ($p<0.05$). Appropriate therapy within 24 h of BSI onset was significantly lower in the *C. striatum* group (28%) compared to the MRSA (64.5%) and MRSE (65.9%) groups ($p<0.005$). The 28-day mortality was higher in the *C. striatum* group (52.0%) compared to the MRSA (25.8%) and MRSE (18.2%) groups.

Conclusions Given the distinct characteristics of *C. striatum*-BSI, including a longer time to positivity than other Gram-positive bacteria and higher mortality rates, we suggest prescribing early appropriate antibiotics if *C. striatum*-BSI is suspected.

Keywords *Corynebacterium striatum*, MRSA, MRSE, Bloodstream infection, Early appropriate antibiotics

Background

Corynebacterium striatum (*C. striatum*), like *Staphylococcus epidermidis*, is a commensal organism of normal human skin and mucosal membranes [1–3]. Historically, *C. striatum* has been regarded by clinicians as a contaminant in blood cultures [4]. Increasingly, it is being recognized as a potential pathogen that can cause a variety of infections in both immunocompromised and immunocompetent hosts [5–7]. Furthermore, *C. striatum* frequently exhibits multidrug resistance, resulting in empirical antibiotic treatment failure [2, 8]. Among the true infections, bloodstream infections

*Correspondence:
Jin-Min Peng
pjm731@hotmail.com
Bin Du
dubin98@gmail.com
[1] Medical Intensive Care Unit, State Key Laboratory of Complex Severe and Rare Diseases, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, 1 Shuai Fu Yuan, Beijing 100730, China
[2] Department of Clinical Laboratory, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China

(BSIs) have been associated with significant mortality and morbidity up to 34% [9, 10].

Current literature on this topic primarily consisted of case reports or case series describing infections at various sites instead of solely focusing on bloodstream infections [11–14]. In addition, previous studies have mainly delineated the microbiological characteristics and resistance profiles of *C. striatum* infections [15, 16], with limited data available on the clinical features and prognosis in real-world clinical settings.

When *C. striatum* is isolated from blood cultures, this finding is usually considered contamination rather than a true infectious pathogen. Clinicians have limited knowledge about positive *C. striatum* blood cultures, including the time to positivity and the usage of antibiotics. The aim of this study was to investigate the clinical characteristics, treatments and outcomes of *C. striatum* BSIs. We compared *C. striatum* BSIs with Methicillin-resistant *Staphylococcus aureus* (MRSA) BSIs and Methicillin-resistant *Staphylococcus epidermidis* (MRSE) BSIs since they are also common skin commensals with similar antibiotic susceptibilities. We aimed to improve the understanding of bloodstream infection caused by this organism and assist clinicians in making clinical decisions.

Methods

Study population and design

A retrospective study of adult hospitalized patients with blood cultures positive for *C. striatum* was conducted at Peking Union Medical College Hospital, a tertiary-care hospital in Beijing, China, between January 2014 and June 2022. A blood culture set consists of one aerobic and one anaerobic blood culture bottle; the amount of blood drawn from patients was about 8 ml (see Supplemental file 1). Coinfection was excluded from the study.

Using electronic medical records, the following data were collected: demographic characteristics, underlying diseases, immunosuppressive status, source of BSI, laboratory tests on the onset of BSI, organ support therapies, antimicrobial therapies, survival time, and outcomes within 28 days from onset of BSI. Charlson comorbidity index score and Pitt bacteremia score were calculated as previous researches [17]. Two qualified physicians looked over patients' medical records to guarantee data consistency.

This study was approved by the Research Ethics Committee of Peking Union Medical College Hospital (PUMCH, K23C1014). As the study was no-interventional and retrospective in nature with anonymized data, the written informed consent and informed consent had been waived.

Definitions

The contaminant group was defined as only one blood culture set that turned positive. Bacteremia was defined as if at least two blood culture sets taken at the same time turned out positive for the same species or when one blood culture specimen and another clinically relevant sample taken from another site yielded positive results. This criteria was applied to *C. striatum*-BSI and MRSE groups due to their characteristics of common skin contaminant [18, 19]. For the MRSA group, patients were categorized as BSI if at least one blood culture set turned out positive. Coinfection was defined as a *C. striatum*-BSI (or MRSE-BSI or MRSA-BSI) with positive blood culture for mixed organisms (bacterial, mycobacterial, or fungal) at the same time.

The onset of BSI was defined as the date of collection of the first blood culture yielded index pathogen. Nosocomial and Intensive care unit (ICU) BSI was defined as the occurrence of BSI in 48 h or more after admission [20]. Neutropenia was defined as an absolute neutrophil count lower than 500/ml at the onset of BSI. Immunosuppressive therapy was defined as a daily dose of $\geq$ 10 mg prednisolone-equivalent steroids, monoclonal antibodies, antimetabolite drugs, or T-cell inhibitors within 30 days before BSI onset. The source of BSI was determined based on an active infection site, and the isolation of the organism from that site coincided with the onset of BSI. The unknown source of infection was BSIs without positive cultures of other body fluids or swab specimens during this infection. Antimicrobial therapy was considered appropriate if at least one active antimicrobial agent, determined by in vitro susceptibility testing, was administered within 24 h after the onset.

Identification and antibiotic susceptibility testing of *Corynebacterium striatum*

C. striatum was identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). Drug susceptibility testing was conducted using the broth microdilution method according to the Clinical and Laboratory Standards Institute guidelines. The antibiotics tested were clindamycin, linezolid, levofloxacin, tigecycline, teicoplanin, penicillin, erythromycin, gentamicin, rifampicin, tetracycline, and vancomycin. For each antibiotic, six dilutions were performed including break points recommended by the CLSI standard and corresponding to the genus Corynebacterium according to the latest edition every year.

Statistical analysis

Data are presented as frequency and percentages for categorical variables and as mean ± standard deviation (SD)

or median with interquartile range (IQR) for continuous variables. Categorical variables were compared using either the Chi-square test or Fisher's exact test, while continuous variables were compared using the Mann–Whitney U test. A *p*-value below 0.05 was considered statistically significant. Data were analyzed using SPSS version 21.0.1. Figures were designed using Prism version 9.0.

Results

Between January 2014 and June 2022, a total of 53 episodes for positive blood culture of *C. striatum* were detected, and 21 cases of these were contaminated and 32 patients were identified as *C. striatum*-BSI. At 32 cases of *C. striatum* infection, 7 cases of these were with coinfection of other microorganisms (Fig. 1). As for the control group, 62 patients with MRSA-BSI, and 44 patients with MRSE-BSI were identified based on the criteria (Fig. 1).

Clinical characteristics of *C. striatum*-BSI group and contaminated group

As shown in Table 1, we observed no significant differences in gender, age, Charlson Comorbidity Index, and underlying health conditions between *C. striatum*-BSI and contaminated group. The time to positivity of blood culture in the contaminated group (42.5 h) was significantly longer ($p=0.011$) than *C. striatum*-BSI group (27 h). *C. striatum* group was in more severe clinical condition according to Pitt bacteremia score (score of 5 vs 3 in median), septic shock (52.0% vs 33.3%), and usage of invasive mechanical ventilation (IMV) (64.0% vs 16.7%) than the contaminated group. The 28-day mortality was higher ($p=0.057$) in *C. striatum* group (52%) than contaminated group(22.2%).

Clinical characteristics of patients with *C. striatum*-BSI

The main characteristics of *C. striatum*-BSI were in (Table 2). *C. striatum*-BSI occurred more frequently in males (70.0%), and the average age of patients was 60 years old. 56.0% of patients were nosocomial infections. The proportion of ICU infection was 20% in *C. striatum*-BSI, 16.1% in MRSA, and 13.6% in MRSE. It was found that the time to BSI onset from hospital admission was longer in *C. striatum*-BSI (14.0 days) than in MRSA (4.0 days) and MRSE groups (6.0 days). We also found that all groups mostly could not find infective sources (64% in *C. striatum*, 43.5% in MRSA, 47.7% in MRSE). As for sources that could be detected, the vascular catheter was the most common site in the *C. striatum* group (16.0%), as well as MRSE (31.8%), and the MRSA group was skin and soft tissue (22.6%). *C. striatum* group (4.0) had a higher ($P=0.007$) Carlson Comorbidity Index compared to the MRSA group (2.0). The proportion of immunocompromised status was 60.0% without statistical difference compared to control groups.

The *C. striatum* group (27.0 h) had a longer time to positivity of blood culture compared to MRSA (20.0 h, $P=0.002$) and MRSE (19.0 h, $P<0.001$) groups. Overall, the clinical condition of the *C. striatum* group (5.0) appeared to be more severe than other groups, as evidenced by a higher Pitt's score compared to the MRSA group (1.0, $P<0.001$) and the MRSE group (1.0, $P<0.001$). Additionally, the *C. striatum* group had normal WBC counts (8.9 X 10^9/L) but lower platelet counts (78.0 X 10^9/L) and a higher incidence of shock (52.0%) compared to control groups. The *C. striatum* group (64%) also had higher utilization of invasive mechanical ventilation than the MRSA (27.4%) and MRSE (25.0%) groups.

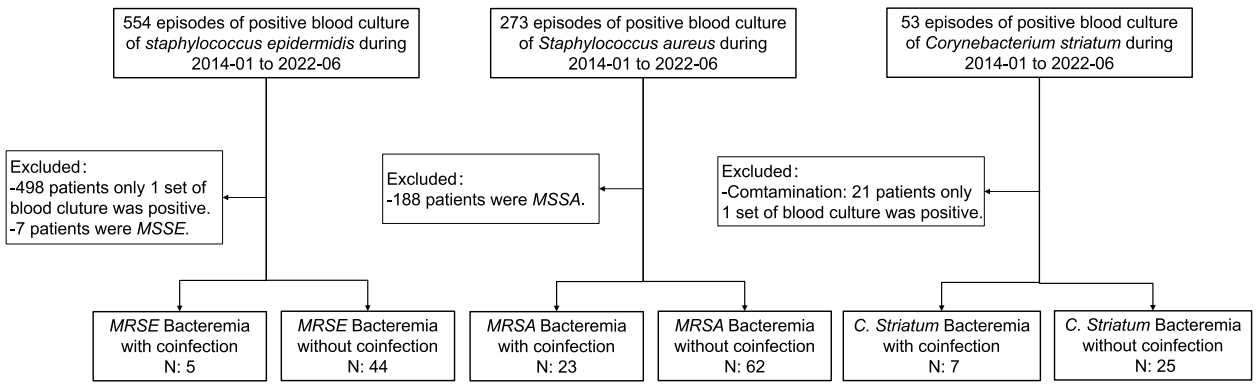

Fig. 1 The study selection of flowchart

Table 1 Patient characteristics of the *C. striatum*-BSI group and contaminated group

Variable	*C. striatum*-BSI	Contaminated	*C. striatum*-BSI vs. Contaminated
	N = 25	*N* = 18[a]	*p* values
Age, [years]	60.0 [39.0, 70.0]	61.0 [49.8, 67.2]	0.657
Male, n (%)	18 (72.0)	9 (50.0)	0.249
Site of BSIs acquisition, n (%)			
Nosocomial infection	14 (56.0)	13 (72.2)	0.444
ICU infection	5 (20.0)	4 (22.2)	1
Time to BSI onset from hospital admission, [days]	14.0 [1.0, 22.0]	6.0 [0.2, 11.2]	0.172
Comorbidities			
Charlson Comorbidity Index	4.0 [2.0, 6.0]	3.5 [1.2, 5.8]	0.544
Diabetes mellitus, n (%)	11 (44.0)	6 (33.3)	0.697
Chronic kidney disease, n (%)	3 (12.0)	3 (16.7)	1
COPD, n (%)	2 (8.0)	3 (16.7)	0.695
Immunocompromised status[b], n (%)	15 (60.0)	10 (55.6)	1
Systemic autoimmune disease	5 (20.0)	15 (24.2)	0.21
Solid tumor	4 (16.0)	8 (44.4)	0.166
Hematology Malignancy	6 (24.0)	1 (5.6)	0.231
Immunosuppressive therapy	10 (40.0)	7 (38.9)	1
Recent surgery within 30 days, n (%)	6 (24.0)	3 (16.7)	0.839
Time to positivity of blood culture, [hours]	27.0 [22.0, 39.0]	42.5 [34.8, 48.8]	0.011
Clinical conditions at BSI onset			
Pitt bacteremia score	5.0 [2.0, 7.0]	0.5 [0.0, 2.8]	0.001
Temperature, [°C]	38.4 (1.6)	37.8 (0.9)	0.141
Septic Shock, n (%)	13 (52.0)	6 (33.3)	0.366
IMV, n (%)	16 (64.0)	3 (16.7)	0.006
CRRT, n (%)	6 (24.0)	2 (11.1)	0.5
Laboratory test			
Platelet, [X 10^9/L]	78.0 [30.0, 125.0]	147.5 [98.8, 291.8]	0.017
WBC, [X 10^9/L]	8.9 [0.9, 12.1]	9.5 [5.7, 14.7]	0.301
Creatinine, [mmol/L]	96.0 [53.0, 288.0]	76.0 [45.5, 174.2]	0.382
Albumin, [g/L]	27.2 (4.3)	30.2 (7.1)	0.102
Outcome			
Length of hospitalization, [days]	10.0 [4.0, 29.0]	14.0 [6.5, 42.5]	0.103
28-days mortality, n (%)	13 (52.0)	4 (22.2)	0.098
In-hospital mortality, n (%)	14 (56.0)	4 (22.2)	0.057

C. striatum, *Corynebacterium striatum*, *BSI* bloodstream infection, *ICU* intensive care unit, *BSI* blood stream infection, *COPD* chronic obstructer pulmonary disease, *IMV* invasive mechanical ventilation, *CRRT* continuous renal replacement therapy, *WBC* white blood cell

Data are presented as n (%) or mean ± SD or median [IQR]; *IQR* interquartile range, *SD* standard deviation

[a] 3 cases missed records among 21 cases

[b] "Immunocompromised" is a composite category of conditions listed below this heading; the conditions listed are not mutually exclusive

Antimicrobial therapy and outcomes of patients with *C. striatum*-BSI

As shown in Table 2, there was a significantly different proportion of appropriate therapy within 24 h in *C. striatum*-BSI (28.0%) compared to MRSA (64.5%) and MRSE (65.9%) groups ($p < 0.05$). Table 3 demonstrated the antibiotics susceptibility. *C. striatum* was mainly susceptible to linezolid, tigecycline, teicoplanin, and vancomycin, consistent with MRSA and MRSE. As shown in Fig. 2, 57.1% (4/7), 44.4% (4/9), and 42.8% (3/7) of patients of *C. striatum*-BSI were prescribed appropriate antibiotics within 24 h after blood culture turned to positivity in a different time to positivity of 0-24 h, 24-36 h, 36-48 h, respectively, which were all lower than MRSA group and MRSE group. The median time to therapy from BSI was two days in the *C. striatum* group, but 1.0 day in

Table 2 Clinical characteristics, treatment and outcome of *C. striatum*-BSI, MRSA-BSI and MRSE-BSI groups

Variable	*C. striatum* *N* = 25	MRSA *N* = 62	MRSE *N* = 44	*C. striatum* vs. MRSA *p* values	*C. striatum* vs. MRSE *p* values
Age, [years]	60.0 [39.0, 70.0]	51.0 [36.5, 63.8]	62.0 [47.2, 72.2]	0.215	0.403
Male, n (%)	18 (72.0)	35 (56.5)	31 (70.5)	0.27	1
Site of BSIs acquisition, n (%)					
Nosocomial infection	14 (56.0)	36 (58.1)	23 (52.3)	0.275	0.962
ICU infection	5 (20.0)	10 (16.1)	6 (13.6)	0.905	0.725
Time to BSI onset from hospital admission, [days]	14.0 [1.0, 22.0]	4.0 [0.0, 13.2]	6.0 [0.0, 20.0]	0.083	0.529
Comorbidities					
Charlson Comorbidity Index	4.0 [2.0, 6.0]	2.0 [1.0, 3.8]	3.0 [2.0, 5.2]	0.007	0.496
Diabetes mellitus, n (%)	11 (44.0)	17 (27.4)	7 (15.9)	0.213	0.023
Chronic kidney disease, n (%)	3 (12.0)	7 (11.3)	7 (15.9)	1	0.930
COPD, n (%)	2 (8.0)	1 (1.6)	2 (4.5)	0.408	0.957
Immunocompromised status[a], n (%)	15 (60.0)	36 (58.1)	19 (43.2)	1	0.275
Systemic autoimmune disease	5 (20.0)	15 (24.2)	3 (6.8)	0.889	0.210
Solid tumor	4 (16.0)	6 (9.7)	12 (27.3)	0.642	0.441
Hematology Malignancy	6 (24.0)	8 (12.9)	4 (9.1)	0.341	0.182
Immunosuppressive therapy	10 (40.0)	22 (35.5)	1 (2.3)	0.881	< 0.001
Recent surgery within 30 days, n (%)	6 (24.0)	16 (25.8)	20 (45.5)	1	0.131
Source of BSI, n (%)					
Vascular catheters	4 (16.0)	6 (9.7)	14 (31.8)	0.642	0.249
Skin and soft tissue	1 (4.0)	14 (22.6)	0 (0.0)	0.078	0.773
Respiratory	3 (12.0)	9 (14.5)	0 (0.0)	1	0.083
Implanted devices[b]	0 (0.0)	4 (6.5)	7 (15.9)	0.463	0.091
Abdominal	1 (4.0)	1 (1.6)	2 (4.5)	1	1
Unknown	16 (64.0)	27 (43.5)	21 (47.7)	0.136	0.293
Time to positivity of blood culture, [hours]	27.0 [22.0, 39.0]	20.0 [15.0, 24.8]	19.0 [14.0, 25.2]	0.002	< 0.001
Clinical conditions at BSI onset					
Pitt bacteremia score	5.0 [2.0, 7.0]	1.0 [0.0, 4.0]	1.0 [0.0, 3.2]	< 0.001	< 0.001
Temperature, [°C]	38.4 (1.6)	38.4 (0.9)	38.5 (0.9)	0.940	0.989
Septic Shock, n (%)	13 (52.0)	24 (38.7)	11 (25.0)	0.371	0.045
IMV, n (%)	16 (64.0)	17 (27.4)	11 (25.0)	0.003	0.003
CRRT, n (%)	6 (24.0)	6 (9.7)	8 (18.2)	0.159	0.790
Laboratory test					
Platelet, [X 10^9/L]	78.0 [30.0, 125.0]	184.5 [93.0, 288.5]	151.0 [101.0, 207.2]	0.003	0.003
White blood cells, [X 10^9/L]	8.9 [0.9, 12.1]	12.3 [7.6, 16.8]	7.8 [4.8, 11.6]	0.040	0.788
Creatinine, [mmol/L]	96.0 [53.0, 288.0]	85.5 [54.2, 152.0]	74.0 [61.8, 168.2]	0.360	0.676
Albumin, [g/L]	27.2 (4.3)	28.3 (5.7)	34.1 (5.8)	0.424	< 0.001
Treatment					
Appropriate therapy within 24 h, n (%)	7 (28.0)	40 (64.5)	29 (65.9)	0.004	0.005
Time to appropriate therapy from onset, [days]	2.0 [1.0, 2.0]	1.0 [0.0, 2.0]	1.0 [0.0, 1.0]	0.060	0.056
Antibiotic therapy, n (%)					
Vancomycin	14 (56.0)	46 (74.2)	34 (81.0)	0.160	0.056
Linezolid	2 (8.0)	5 (8.1)	5 (11.9)	1	0.926
Teicoplanin	1 (4.0)	2 (3.3)	3 (7.1)	1	1
Outcome					
Length of hospitalization, [days]	10.0 [4.0, 29.0]	17.0 [8.8, 28.8]	15.5 [9.0, 27.2]	0.026	0.075
28-days mortality, n (%)	13 (52.0)	16 (25.8)	8 (18.2)	0.036	0.008
In-hospital mortality, n (%)	14 (56.0)	17 (27.4)	9 (20.5)	0.023	0.006

C. striatum, *Corynebacterium striatum*, *BSI* blood stream infection, *MRSA* Methicillin-resistant *Staphylococcus aureus, MRSE* Methicillin-resistant *Staphylococcus epidermidis*, *ICU* intensive care unit, *COPD* chronic obstructer pulmonary disease, *IMV* invasive mechanical ventilation, *CRRT* continuous renal replacement therapy, *WBC* white blood cell

Data are presented as n (%) or mean ± SD or median [IQR]; *IQR* interquartile range; *SD* standard deviation

[a] "Immunocompromised" is a composite category of conditions listed below this heading; the conditions listed are not mutually exclusive

[b] Implanted devices included prosthetic valves, implantable cardioverter defibrillator and stent

Table 3 Drug susceptibility results of *C. striatum, MRSA,* and MRSE group

	Susceptible/tested (%)		
	C. striatum	**MRSA**	**MRSE**
Clindamycin	1/25 (4.0%)	14/59 (23.7%)	23/44 (52.3%)
Erythromycin	10/25 (40.0%)	9/60 (15.0%)	7/43 (16.3%)
Gentamicin	15/25 (60.0%)	40/60 (66.7%)	24/44 (54.5%)
Linezolid	25/25 (100%)	60/60 (100%)	43/43 (100%)
Levofloxacin	0/25 (0%)	27/44 (61.4%)	16/40 (40.0%)
Penicillin	6/25 (24.0%)	0/62 (0%)	1/44 (2.2%)
Rifampicin	13/25 (52.0%)	54/59 (91.5%)	35/44 (79.5%)
Co-trimoxazole	0/25 (0%)	51/60 (85%)	18/44 (40.9%)
Tetracycline	10/25 (40.0%)	11/36 (30.6%)	19/24 (79.2%)
Tigecycline	25/25 (100%)	41/41 (100%)	39/39 (100%)
Teicoplanin	5/5 (100%)	59/59 (100%)	41/41 (100%)
Vancomycin	25/25 (100%)	60/60 (100%)	43/43 (100%)

the MRSA and MRSE groups. The most frequently used antibiotics in all groups were vancomycin, accounting for more than half of the cases. No significant differences were observed between the groups using vancomycin, linezolid, or teicoplanin.

We found the 28-day mortality and in-hospital mortality among the *C. striatum* group (52.0% and 56.0%, respectively) were higher than MRSA (25.8% and 27.4%, respectively) and MRSE (18.2% and 20.5%, respectively) groups, significant differences were observed in both comparisons.

Table 4 showed the factors associated with 28-day mortality in *C. striatum*-BSI, and septic shock was the univariable risk factor for mortality. The proportion of appropriate therapy within 24 h was 33.3% and 23.1% in survivors and non-survivors.

Discussion

We conducted a retrospective study among hospitalized patients with *C. striatum*-positive blood cultures, revealing a bacteremia rate of 60.4%(32/53) using a stringent diagnostic criteria. Among these confirmed bloodstream infections, *C. striatum* was mainly susceptible to vancomycin, linezolid, teicoplanin, and tigecycline. The proportion of *C. striatum* cases that received timely appropriate antibiotics was less than 30%, significantly lower compared to MRSA-BSI and MRSE-BSI, despite similar antibiotic susceptibility profiles. Furthermore, the observed 28-day mortality rate was 52%, notably higher than that of MRSA and MRSE.

C. striatum is commonly considered a contaminant in positive blood culture. Recent literature reported its contamination rates ranging from 29% to 42% [4, 6, 21]. Differences in these rates could be due to varying criteria used to ascertain contamination. Our observed contamination rate was 39.6% (21/53), relatively elevated, likely due to the adoption of more stringent criteria. This rate aligned with Yanai and colleagues' study that applied the same criteria [10]. Patients identified as contaminants in our cohort had significantly longer time to positivity compared to the contaminated group (42.5h vs 27.0h) and displayed markedly lower 28-day mortality rates as well (52.0% vs 22.2%). These findings collectively support the precision in identifying this cohort of contaminated patients.

As for *C. striatum* BSIs, patients with immunocompromised status were 60%. This was accordant with Ishiwada and colleagues' study, which showed 54% of *C. striatum* BSIs were under malignancy, and this rate was 46.4% in Yanai and colleagues' research [10, 15]. Abe and colleagues' research identified 147 cases of Corynebacterium bacteremia in patients with hematological disorders [5]. In our study, 64% of *C. striatum*-BSIs had no primary source of infection, which was slightly higher than the

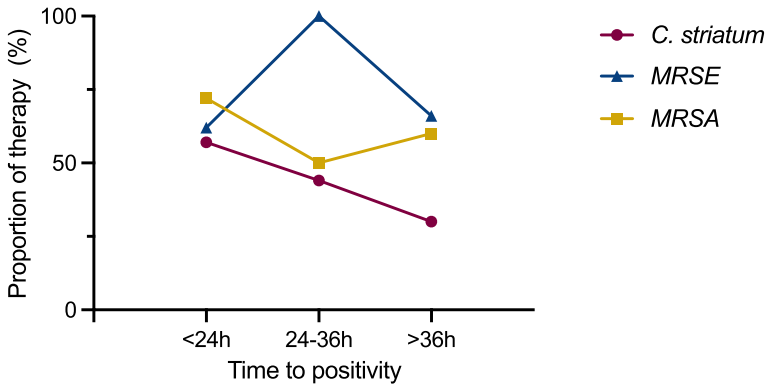

Fig. 2 Initiation of appropriate treatment within 24h since positivle culture according to time to positivity

Table 4 Patient characteristics of survivors and non-survivors in *C. striatum*-BSI

Variable	Survivors *N* = 12	Non-survivors *N* = 13	*p* value
Age, [years]	58.0 [36.5, 67.0]	62.0 [46.0, 74.0]	0.549
Male, n (%)	9 (75.0)	9 (69.2)	1
Nosocomial infection, n (%)	7 (58.3)	7 (53.8)	1
ICU infection, n (%)	2 (16.7)	3 (23.1)	1
Time to BSI onset from admission, [days]	7.5 [0.8, 18.2]	14.0 [1.0, 36.0]	0.38
Comorbidities, n (%)			
Charlson Comorbidity Index	4.0 [2.8, 5.2]	5.0 [2.0, 7.0]	0.603
Diabetes mellitus	4 (33.3)	7 (53.8)	0.529
Chronic kidney disease	2 (16.7)	1 (7.7)	0.941
COPD	0 (0.0)	2 (15.4)	0.497
Immunocompromised status[a], n (%)	6 (50.0)	9 (69.2)	0.567
Source of infection, n (%)			
Vascular catheters	3 (25.0)	1 (7.7)	0.527
Skin and soft tissue	1 (8.3)	0 (0.0)	0.967
Respiratory	1 (8.3)	2 (15.4)	1
Abdominal	1 (8.3)	0 (0.0)	0.967
Unknown	6 (50.0)	10 (76.9)	0.325
Time to the first blood culture positivity, [hours]	28.5 [21.5, 38.0]	26.0 [25.0, 46.0]	0.743
Clinical conditions at BSI onset			
Pitt bacteremia score	3.0 [1.0, 4.2]	6.0 [5.0, 8.0]	0.007
Temperature, °C	38.5 (1.3)	38.4 (1.9)	0.919
Septic shock, n (%)	3 (25.0)	10 (76.9)	0.028
IMV, n (%)	8 (66.7)	8 (61.5)	1
CRRT, n (%)	4 (33.3)	2 (15.4)	0.561
Laboratory test			
Platelet, [X 109/L]	72.5 [39.0, 172.8]	78.0 [23.0, 121.0]	0.624
WBC, [X 109/L]	10.0 [7.1, 13.1]	3.6 [0.3, 11.1]	0.514
Creatinine, [mmol/L]	162.0 [63.8, 259.5]	64.0 [49.0, 293.0]	0.48
Albumin, [g/L]	27.2 (2.8)	27.3 (5.5)	0.937
Treatment			
Appropriate therapy within 24 h, n (%)	4 (33.3)	3 (23.1)	0.901
Time to therapy from BSI onset, [days]	1.5 [1.0, 2.0]	2.0 [0.8, 2.0]	0.956
Vancomycin, n (%)	9 (75.0)	5 (38.5)	0.151

Abbreviations: *C. striatum*, *Corynebacterium striatum*, *BSI* blood stream infection, *ICU* intensive care unit, *COPD* chronic obstructer pulmonary disease, *IMV* invasive mechanical ventilation, *CRRT* continuous renal replacement therapy, *WBC* white blood cell

Data are presented as n (%) or mean ± SD or median [IQR]; IQR, interquartile range; SD, standard deviation

[a] "Immunocompromised" is a composite category of conditions listed below this heading; the conditions listed are not mutually exclusive

40–53% reported in previous studies [9, 15]. This high proportion was reliable because we applied strict criteria for *C. striatum*-BSI with unknown origin, requiring two sets of positive blood cultures from different sites at the same time. Furthermore, since these patients presented with symptoms of infection, comprehensive screening for infection foci was conducted at the time of blood culture collection following the standard protocol. This result reflected the difficulty in identifying the primary infection sites for *C. striatum*-BSI and suggested that cases with *C. striatum* positive blood cultures but without definitive primary infection sites should be took into account to *C. striatum*-BSIs when patients had compatible clinical symptoms and had undergone comprehensive infection focus screening. The most common primary infection site of *C. striatum*-BSIs was catheter-related in our study, accounting for 16%, consistent with similar proportions of 19% found in previous studies [9, 15]. In contrast, implants and skin/soft tissues were the most common primary infection sites for MRSE-BSIs and

MRSA-BSIs, which were rational to their clinical characteristics [22, 23].

In our study, the average time to blood culture positivity for *C. striatum* BSI was 27 h, which was longer than that observed in the control groups of MRSE-BSI (19 h) and MRSA-BSI (20 h). This difference could be attributed to the high proportion of immuncompromsied pateints in the *C. striatum* BSI group, who were more susceptible to infections even at lower bacterial loads. Although a longer time to positivity often implies contamination, the likelihood of mistaking contamination for bacteremia is low due to our study's stringent criteria for the diagnosis of *C. striatum* BSI. Additionally, similar findings were reported in the studies by Ishiwada and Watanabe [15, 21]. The prolonged time to positivity in *C. striatum* BSI may lead to the suspicion of contamination, resulting in delayed antibiotic usage [24], as demonstrated in this study.

Patients with *C. striatum* BSI experienced worse clinical outcomes. In recent years, some outbreaks of nosocomial infections of *C. striatum* were reported, particularly among patients with chronic diseases, exposure to broad-spectrum antibiotics and longtime stay in hospital [2, 25–27]. The mortality of *C. striatum*-BSI in this study was two times higher than control groups. Meanwhile, *C. striatum*-BSI had a higher incidence of shock and was more likely to require invasive mechanical ventilation. The reported mortality of *C. striatum*-BSI was approximately 34% [9], which was lower than the 56% observed in this study. The high mortality is attributed to multiple factors. Firstly, there is a high proportion of immunocompromised patients in *C. striatum*-BSI patients, facing a higher risk of poor outcomes [28, 29]. Secondly, unlike most MRSA-BSI and MRSE-BSI with known primary infection foci, a high proportion of *C. striatum* BSI did not have identifiable infection sites, which are recognized to be related to a higher risk of severe organ dysfunction and mortality [30]. Thirdly, high mortality was associated with only a 28% rate of early appropriate antibiotic therapy and a long time interval from the onset of BSI to the initiation of appropriate treatment. These findings may be partially due to several reasons. The longer time to positivity could delay the early prescription. However, regardless of the time to positivity, only 43–57% of *C. striatum* BSI received appropriate therapies. This indicated that clinicians should be more aware of *C. striatum*-BSI. Furthermore, *C. striatum* was a multidrug-resistant pathogen [31]. Previous studies have demonstrated that *C. striatum* was resistant to many common antibiotics, such as cephalosporins, and only susceptible to a few antibiotics, such as linezolid, vancomycin, and teicoplanin [32, 33], which could lead to a lower rate of appropriate empiric antibiotic therapy.

Our study has some limitations. Due to the lack of a generally accepted definition, we could not precisely distinguish between true BSI with *C. striatum* and contamination cases. We applied a stringent definition for *C. striatum*-BSIs, which may carry the potential risk of misclassifying actual infections as contaminations. Nevertheless, the notable difference in mortality and disease severity between these two groups supports the appropriateness of the definition used in this study. Secondly, the study was conducted retrospectively at a single center, which may limit the generalizability of the findings to other settings. The limited number of cases hindered our exploration of risk factors associated with the prognosis of *C. striatum*-BSI.

In conclusion, we found the rate of *C. striatum* bacteremia was 60.4% among the positive blood cultures for *C. striatum*. *C. striatum* bacteremia is more common in immunocompromised patients, with a low proportion of appropriate antibiotics and a high mortality. Clinicians should pay full attention to *C. striatum* bacteremia and not easily regard positive blood cultures of Gram-positive bacilli as contamination.

Abbreviations

C. striatum	*Corynebacterium striatum*
BSIs	Bloodstream infections
MRSA	Methicillin-resistant *Staphylococcus aureus*
MRSE	Methicillin-resistant *Staphylococcus epidermidis*
ICU	Intensive care unit
IMV	Invasive mechanical ventilation
COPD	Chronic obstructer pulmonary disease
CRRT	Continuous renal replacement therapy
WBC	White blood cell
IQR	Interquartile range
SD	Standard deviation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-09883-z.

Supplementary Material 1.

Acknowledgements

We thank our team at Medical Intensive Care Unit, Peking Union Medical College Hospital.

Author's contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Shu-hua He, Jin-min Peng and Bin Du. The first draft of the manuscript was written by Shu-hua He and Jin-min Peng, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding

We acknowledge the support from.

1. National Key R&D Program of China from Ministry of Science and Technology of the People's Republic of China (2022YFC2304601, 2021YFC2500801) by Bin Du.

2. CAMS Innovation Fund for Medical Sciences (CIFMS) 2021-I2M-1–062 from Chinese Academy of Medical Sciences by Bin Du.

3. National High Level Hospital Clinical Research Funding(2022-PUMCH-D-005, 2022-PUMCH-D-111, 2022-PUMCH-B-126) by Bin Du.
4. National key clinical specialty construction projects from National Health Commission by Bin Du.

Availability of data and materials
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Research Ethics Committee of Peking Union Medical College Hospital (PUMCH, K23C1014). The Research Ethics Committee of Peking Union Medical College Hospital waived the requirement for informed consent owing to the non-interventional, retrospective study design.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 11 April 2024 Accepted: 5 September 2024
Published online: 17 September 2024

References

1. Funke G, von Graevenitz A, Clarridge JE, Bernard KA. Clinical microbiology of coryneform bacteria. Clin Microbiol Rev. 1997;10(1):125–59. https://doi.org/10.1128/CMR.10.1.125.
2. Silva-Santana G, Silva CMF, Olivella JGB, 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(5):1863–80. https://doi.org/10.1007/s00203-021-02246-1.
3. Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. Nature. 2012;486(7402):207–14. https://doi.org/10.1038/nature11234.
4. Rasmussen M, Mohlin AW, Nilson B. From contamination to infective endocarditis—a population-based retrospective study of Corynebacterium isolated from blood cultures. Eur J Clin Microbiol Infect Dis. 2020;39(1):113–9. https://doi.org/10.1007/s10096-019-03698-6.
5. Abe M, Kimura M, Maruyama H, et al. Clinical characteristics and drug susceptibility patterns of Corynebacterium species in bacteremic patients with hematological disorders. Eur J Clin Microbiol Infect Dis. 2021;40(10):2095–104. https://doi.org/10.1007/s10096-021-04257-8.
6. Kimura S, Gomyo A, Hayakawa J, et al. Clinical characteristics and predictive factors for mortality in coryneform bacteria bloodstream infection in hematological patients. J Infect Chemother. 2017;23(3):148–53. https://doi.org/10.1016/j.jiac.2016.11.007.
7. Garcia CM, McKenna J, Fan L, Shah A. Corynebacterium Striatum Bacteremia in End-Stage Renal Disease: A Case Series and Review of Literature. R I Med J (2013). 2020;103(8):46–9.
8. Tang J, Kornblum D, Godefroy N, et al. Corynebacterium striatum thrombophlebitis: a nosocomial multidrug-resistant disease? Access Microbiol. 2021;3(12): 000307. https://doi.org/10.1099/acmi.0.000307.
9. Yamamuro R, Hosokawa N, Otsuka Y, Osawa R. Clinical Characteristics of Corynebacterium Bacteremia Caused by Different Species, Japan, 2014–2020. Emerg Infect Dis. 2021;27(12):2981–7. https://doi.org/10.3201/eid2712.210473.
10. Yanai M, Ogasawasa M, Hayashi Y, Suzuki K, Takahashi H, Satomura A. Retrospective evaluation of the clinical characteristics associated with Corynebacterium species bacteremia. Braz J Infect Dis. 2018;22(1):24–9. https://doi.org/10.1016/j.bjid.2017.12.002.
11. Oliva A, Belvisi V, Iannetta M, et al. Pacemaker lead endocarditis due to multidrug-resistant Corynebacterium striatum detected with sonication of the device. J Clin Microbiol. 2010;48(12):4669–71. https://doi.org/10.1128/JCM.01532-10.
12. Kalt F, Schulthess B, Sidler F, et al. Corynebacterium Species Rarely Cause Orthopedic Infections. J Clin Microbiol. 2018;56(12):e01200-e1218. https://doi.org/10.1128/JCM.01200-18.
13. Sturm PDJ, Scholle D. Arthritis caused by Corynebacterium striatum: spontaneous infection? J Clin Microbiol. 2007;45(6):2097. https://doi.org/10.1128/JCM.00298-07. author reply 2097.
14. Ge Y, Lu J, Feng S, Ji W, Tong H. A case of catheter related bloodstream infection by Corynebacterium striatum. IDCases. 2020;22: e00987. https://doi.org/10.1016/j.idcr.2020.e00987.
15. Ishiwada N, Watanabe M, Murata S, Takeuchi N, Taniguchi T, Igari H. Clinical and bacteriological analyses of bacteremia due to Corynebacterium striatum. J Infect Chemother. 2016;22(12):790–3. https://doi.org/10.1016/j.jiac.2016.08.009.
16. Milosavljevic MN, Milosavljevic JZ, Kocovic AG, et al. Antimicrobial treatment of Corynebacterium striatum invasive infections: a systematic review. Rev Inst Med Trop Sao Paulo. 2021;63: e49. https://doi.org/10.1590/S1678-9946202163049.
17. Chow JW, Yu VL. Combination antibiotic therapy versus monotherapy for gram-negative bacteraemia: a commentary. Int J Antimicrob Agents. 1999;11(1):7–12. https://doi.org/10.1016/S0924-8579(98)00060-0.
18. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control. 2008;36(5):309–32. https://doi.org/10.1016/j.ajic.2008.03.002.
19. Osaki S, Kikuchi K, Moritoki Y, et al. Distinguishing coagulase-negative Staphylococcus bacteremia from contamination using blood-culture positive bottle detection pattern and time to positivity. J Infect Chemother. 2020;26(7):672–5. https://doi.org/10.1016/j.jiac.2020.02.004.
20. Sathaporn N, Khwannimit B. Risk Factor for Superimposed Nosocomial Bloodstream Infections in Hospitalized Patients with COVID-19. Infect Drug Resist. 2023;16:3751–9. https://doi.org/10.2147/IDR.S411830.
21. Watanabe N, Otsuka Y, Watari T, Hosokawa N, Yamagata K, Fujioka M. Time to positivity of Corynebacterium in blood culture: Characteristics and diagnostic performance. PLoS ONE. 2022;17(12): e0278595. https://doi.org/10.1371/journal.pone.0278595.
22. Lakhundi S, Zhang K. Methicillin-Resistant Staphylococcus aureus: Molecular Characterization, Evolution, and Epidemiology. Clin Microbiol Rev. 2018;31(4):e00020-e118. https://doi.org/10.1128/CMR.00020-18.
23. Kleinschmidt S, Huygens F, Faoagali J, Rathnayake IU, Hafner LM. Staphylococcus epidermidis as a cause of bacteremia. Future Microbiol. 2015;10(11):1859–79. https://doi.org/10.2217/fmb.15.98.
24. Ruiz-Giardín JM, Martin-Díaz RM, Jaqueti-Aroca J, Garcia-Arata I, San Martín-López JV, Sáiz-Sánchez BM. Diagnosis of bacteraemia and growth times. Int J Infect Dis. 2015;41:6–10. https://doi.org/10.1016/j.ijid.2015.10.008.
25. Verroken A, Bauraing C, Deplano A, et al. Epidemiological investigation of a nosocomial outbreak of multidrug-resistant Corynebacterium striatum at one Belgian university hospital. Clin Microbiol Infect. 2014;20(1):44–50. https://doi.org/10.1111/1469-0691.12197.
26. Leonard RB, Nowowiejski DJ, Warren JJ, Finn DJ, Coyle MB. Molecular evidence of person-to-person transmission of a pigmented strain of Corynebacterium striatum in intensive care units. J Clin Microbiol. 1994;32(1):164–9. https://doi.org/10.1128/jcm.32.1.164-169.1994.
27. Renom F, Garau M, Rubí M, Ramis F, Galmés A, Soriano JB. Nosocomial outbreak of Corynebacterium striatum infection in patients with chronic obstructive pulmonary disease. J Clin Microbiol. 2007;45(6):2064–7. https://doi.org/10.1128/JCM.00152-07.
28. Elting LS, Rubenstein EB, Rolston KV, Bodey GP. Outcomes of bacteremia in patients with cancer and neutropenia: observations from two decades of epidemiological and clinical trials. Clin Infect Dis. 1997;25(2):247–59. https://doi.org/10.1086/514550.
29. Nørgaard M, Larsson H, Pedersen G, Schønheyder HC, Sørensen HT. Risk of bacteraemia and mortality in patients with haematological malignancies. Clin Microbiol Infect. 2006;12(3):217–23. https://doi.org/10.1111/j.1469-0691.2005.01298.x.
30. Gupta S, Sakhuja A, Kumar G, McGrath E, Nanchal RS, Kashani KB. Culture-Negative Severe Sepsis: Nationwide Trends and Outcomes. Chest. 2016;150(6):1251–9. https://doi.org/10.1016/j.chest.2016.08.1460.

31. Kang Y, Chen S, Zheng B, et al. Epidemiological Investigation of Hospital Transmission of Corynebacterium striatum Infection by Core Genome Multilocus Sequence Typing Approach. Van Tyne D, ed. Microbiol Spectr. 2023;11(1):eo1490-22. https://doi.org/10.1128/spectrum.01490-22.
32. Ramos JN, Souza C, Faria YV, et al. Bloodstream and catheter-related infections due to different clones of multidrug-resistant and biofilm producer Corynebacterium striatum. BMC Infect Dis. 2019;19(1):672. https://doi.org/10.1186/s12879-019-4294-7.
33. Cc D, Be L, Il C, et al. Antimicrobial Susceptibility Testing for Corynebacterium Species Isolated from Clinical Samples in Romania. *Antibiotics (Basel, Switzerland)*. 2020;9(1). https://doi.org/10.3390/antibiotics9010031.

Publisher's Note