

Outcome of Corynebacterial Bloodstream Infection in Patients With Cardiac Implantable Electronic Devices: A Brief Report and Systematic Review

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Cardiac implantable electronic device infection in the context of corynebacterial bloodstream infection (BSI) remains poorly understood. From 2012 to 2023 at Mayo Clinic, 4 of 12 patients with corynebacterial BSI had cardiac implantable electronic device infection: 1 patient was diagnosed during a relapsing BSI episode. Undefined source, persistent BSI, and the presence of a prosthetic cardiac valve were common characteristics.

Keywords. bloodstream infection; cardiac implantable electronic device; *Corynebacterium*; infection; relapse.

Cardiac implantable electronic device infection (CIEDI) has dramatically increased worldwide, particularly among individuals with significant medical comorbidities [1–3]. Bloodstream infections (BSIs) in patients with cardiac implantable electronic devices (CIEDs) are a challenging clinical entity, as they may be a marker of underlying CIEDI [4]. The propensity for CIEDI in patients who present with BSI varies with the type of pathogen involved, as demonstrated in previous studies [5–9]. Staphylococci, for example, are responsible for the majority of CIEDIs, accounting for up to 50%, while other pathogens

present a lower risk of CIEDI in the context of BSI. Data are sparse on the risk of CIEDI with less common organisms, such as *Corynebacterium* species.

Corynebacterium species, an aerobic gram-positive bacillus, has traditionally been dismissed as a contaminant in many clinical settings due to its presence in the skin microbiota [10, 11]. In a population-based cohort study, only 8% of all positive blood cultures with *Corynebacterium* species represented true BSI [12]. However, it has recently emerged as a significant pathogen in specific populations, including patients who are immunocompromised and those with prosthetic devices [12–14]. CIEDIs with *Corynebacterium* species are notably rare. Most studies have documented CIEDI due to this species by cultures of extracted devices rather than by BSI [15–17]. This study aims to investigate all patients with CIED who presented with corynebacterial BSI and all prior reported cases from a systematic review.

METHODS

Population

All patients aged ≥ 18 years with CIED who were hospitalized at Mayo Clinic in Minnesota, Arizona, and Florida due to corynebacterial BSI from 1 January 2012 to 31 December 2023 were reviewed. Patients who had a left ventricular assist device were excluded. All variables were manually abstracted from electronic medical records.

Definitions

Corynebacterial BSI was defined as the growth of *Corynebacterium* species in at least 2 sets of blood cultures. Polymicrobial BSIs were excluded. CIEDI due to *Corynebacterium* species was defined by (1) signs of pocket site infection, (2) the presence of lead or valve vegetation in the setting of corynebacterial BSI, or (3) relapsing corynebacterial BSI within 90 days without a distinct diagnosis [18–21]. Relapsing BSI was defined as a new episode of BSI with the same species of *Corynebacterium*. CIEDI status was “unknown” if patients did not undergo appropriate investigation for CIEDI. Duration of BSI was defined as the duration from the first day of positive blood culture until the first day of negative blood culture. Duration of BSI > 3 days was defined as a persistent BSI. Community-onset BSI and time to positivity were previously defined [6].

Microbiology

After the organisms were subcultured from blood cultures, matrix-assisted laser desorption ionization–time of flight mass spectrometry (Bruker Daltonics Inc) was used for species identification. When indicated, additional morphologic and biochemical traits or partial 16S rRNA gene sequencing were used. Susceptibility testing was performed with agar dilution

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methods (for penicillin, ceftriaxone, meropenem, and vancomycin) in accordance with the Clinical and Laboratory Standards Institute guidelines.

Objectives

The primary objective of this study was to analyze the clinical characteristics and 90-day outcomes of patients with CIED and corynebacterial BSI. Additionally, the secondary objective was to conduct a systematic review of all cases of CIEDI due to corynebacterial BSI in existing literature.

Patient Consent Statement

The study was approved by the Mayo Clinic Institutional Review Board (20-009376). Individual written informed consent was waived. Minnesota patients without research authorization were excluded.

Systematic Review

A comprehensive search of MEDLINE, Embase, Science Citation Index, Emerging Sources Citation Index, SCOPUS, and Google Scholar was performed on 8 February 2024 by an experienced librarian (M.T.M.). Date limits were restricted to 2000 to 2023. Case reports, case series, or individual cases from cohort studies that reported corynebacterial BSI in patients with CIED were screened.

Statistical Analysis

Descriptive statistics were used and reported as median (IQR) for continuous variables and count (percentage) for categorical variables. All analyses were performed with BlueSky Statistics version 10.3.1 (BlueSky Statistics LLC).

RESULTS

Our Cohort

A total of 61 patients with CIED had a positive blood culture for *Corynebacterium* species during the study period. Of those, 49 patients were excluded: 46 had contaminated blood cultures and 3 had a left ventricular assist device. Twelve patients were included in the study (Table 1).

Baseline Demographics

The median age was 70.3 years (IQR, 53.5–80.6) with 66.7% male and 91.7% White. Five (41.7%) patients had diabetes mellitus; 3 (25.0%) had end-stage kidney disease requiring hemodialysis; and 3 (25.0%) had histories of hematologic malignancies. Cardiac comorbidities were common: 8 (66.7%) with valve abnormalities and 6 (50.0%) with prosthetic cardiac valves. Other cardiac comorbidities included 9 (75.0%) with heart failure and 8 (66.7%) with coronary artery diseases. Type of CIED included 6 (50.0%) with an implantable cardioverter-defibrillator, 5 (41.7%) with a permanent pacemaker, and 1 (8.3%) with cardiac resynchronization therapy.

None had a history of CIEDI or a prior BSI episode. The median time from device implantation to BSI was approximately 2 years (752 days; IQR, 72.8–1341.0).

Microbiology

Corynebacterium species included *C striatum* (n = 9, 75.0%), *C jeikeium* (n = 2, 16.7%), and *C glucuronolyticum* (n = 1, 8.3%). Susceptibility testing was available in 10 patients: all isolates were vancomycin susceptible while only 2 were penicillin susceptible. The median time to positivity was 23 hours (IQR, 19.5–27.5).

Clinical Courses

Eleven (91.7%) BSIs were community onset. Only 4 (33.3%) patients had fever during the time of BSI. None had signs of pocket site infection. Undefined source of infection was the most common (n = 6, 50.0%), followed by 2 central line-associated BSIs, 2 skin/soft tissue infections, 1 infected arteriovenous fistula, and 1 urinary source. Among 10 patients who had follow-up blood culture, 5 (50.0%) had persistent BSI. The median duration of BSI was 3.5 days (IQR, 2.0–4.0).

All but 1 patient (91.7%) underwent echocardiography: 5 (45.5%) had transthoracic and transesophageal echocardiography, 5 (45.5%) had only transthoracic, and 1 (9.1%) had only transesophageal. Two patients had positive echocardiographic findings (Table 1). One patient underwent [¹⁸F]-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT), which demonstrated uptake at the aortic root graft and prosthetic aortic valve.

Outcomes

Three (25.0%) patients died shortly after developing BSI (Nos. 1, 4, and 9), and their CIEDI status was unknown.

CIEDI was diagnosed in 3 (25.0%) patients (Nos. 5, 7, and 11). Two of 3 patients with CIEDI (66.7%; Nos. 7 and 11) underwent redo sternotomy aortic valve/graft replacement and CIED extraction. Tissue and device cultures from both patients grew *Corynebacterium* species. Both received intravenous vancomycin after device extraction. The remaining patient with CIEDI (No. 5) died in hospice soon after CIEDI diagnosis.

Six patients (50.0%; Nos. 2, 3, 6, 9, 10, and 12) who were not diagnosed with CIEDI received intravenous vancomycin or oral linezolid ranging from 2 to 6 weeks (Table 1). All of them survived beyond 90 days. One patient (No. 3) developed relapsing BSI with the same *Corynebacterium* species within 90 days. The repeat transesophageal echocardiography finding was negative, and PET/CT was not done. The patient was treated with 4 weeks of intravenous vancomycin, followed by oral linezolid daily suppression, for a presumed CIEDI. At the most recent follow-up visit, 8 months after the relapsed BSI episode, the patient had tolerated linezolid without any side effects.

Table 1. Clinical Characteristics and Outcomes of Patients With CIEDs Who Developed Corynebacterial BSIs at Our Institution: 2012–2023

No.	Age, y; Sex	CIED; Prosthetic Cardiac Valve	<i>Corynebacterium</i> sp; source	Duration of BSI, d	TTE Finding; TEE Finding	CIEDI	Antibiotic; Duration of Antibiotic, d	Complete CIED Extraction	Death; Relapse (Within 90 d)	Comments
1	97; F	PPM; yes (aortic)	<i>C striatum</i> ; undefined	No follow-up blood culture obtained	Negative; not done	Unknown	NA; 0	No	Yes; NA	Died soon after BSI
2	77; F	PPM; no	<i>C striatum</i> ; infected arteriovenous fistula	3	Negative; not done	No	Linezolid; 13	No	No; no	...
3	92; F	ICD; yes (aortic and mitral)	<i>C striatum</i> ; undefined	2	Negative; negative	No	Vancomycin; 13	No	No; yes	Relapsed episode ^a
4	68; M	ICD; yes (aortic)	<i>C striatum</i> ; undefined	No follow-up blood culture obtained	Not done; not done	Unknown	NA; 0	No	Yes; NA	Died soon after BSI
5	54; F	ICD; no	<i>C jeikeium</i> ; central line	4	Negative; vegetation at the right atrium portion of CIED lead	Yes	Vancomycin; 23	No	Yes; no	Died soon after CIEDI diagnosis
6	79; M	PPM; no	<i>C glucuronolyticum</i> ; urinary tract	2	Negative; not done	No	Vancomycin; 15	No	No; no	...
7	37; M	CRT; yes (aortic)	<i>C striatum</i> ; undefined	1	Negative; negative	Yes	Vancomycin; 76	Yes	No; no	Diagnosed by PET/CT
8	53; M	ICD; no	<i>C striatum</i> ; skin and soft tissue	5	Not done; negative	No	Vancomycin; 50	No	No; no	...
9	54; M	ICD; no	<i>C striatum</i> ; central line	5	Negative; not done	Unknown	Vancomycin; 5	No	Yes; NA	Died soon after BSI
10	85; M	PPM; yes (aortic)	<i>C striatum</i> ; undefined	1	Negative; not done	No	Vancomycin then linezolid; 10	No	No; no	...
11	41; M	PPM; yes (aortic)	<i>C jeikeium</i> ; undefined	4	Mobile density on prosthetic aortic and native mitral valve; vegetations on aortic and mitral valves with aortic root abscess	Yes	Vancomycin; 42	Yes	No; no	...
12	72; M	ICD; no	<i>C striatum</i> ; skin and soft tissue	4	Negative; negative	No	Vancomycin; 28	No	No; no	...

Abbreviations: BSI, bloodstream infection; CIED, cardiac implantable electronic device; CIEDI, cardiac implantable electronic device infection; CRT, cardiac resynchronization therapy; F, female; ICD, implantable cardioverter-defibrillator; M, male; NA, not applicable; PET/CT, [18F]-fluorodeoxyglucose positron emission tomography/computed tomography; PPM, permanent pacemaker; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

^aTreated as CIEDI with device retention and chronic antibiotic suppression.

Prior Reported Cases

A total of 40 articles were reviewed. Eleven studies were included. All of them were a single case report [22–32] (Table 2). Interestingly, 7 of 11 cases had prior episodes of corynebacterial BSI, and CIEDI was diagnosed only during the relapsed episodes. Nine patients underwent CIED extraction with favorable outcomes.

DISCUSSION

This study provides a detailed clinical analysis of 12 patients with CIED who developed corynebacterial BSI over the past

12 years. The findings highlight several critical aspects. First, one-third of our cohort had confirmed CIEDI. Common features of confirmed cases included undefined source of BSI, prosthetic cardiac valve, and persistent BSI. These risk factors are comparable to those of BSI due to common pathogens [33]. Second, one-fourth of our cohort had an undetermined CIEDI status due to mortality from BSI before an appropriate investigation, underscoring the severity of corynebacterial BSI in patients with multiple comorbidities. Prior studies have noted high mortality rates (up to 30%) in patients with BSI from *C striatum* or *C jeikeium*, particularly patients with hematologic malignancies

Table 2. Systematic Review of All Reported Cases of CIEDs With Corynebacterial BSIs, 2000–2023

First Author	Year	Age, y; Sex	CIED; Prosthetic Cardiac Valve	<i>Corynebacterium</i> Sp	Corynebacterial BSI: Prior Episode	Echocardiographic Finding	Complete CIED Extraction	Outcome
Marti [22]	2008	59; M	ICD; yes (aortic)	<i>C xerosis</i>	No	Vegetation on the CIED lead and abscess around the generator	Yes	Survive
Bechara [23]	2011	72; M	PPM; not reported	<i>C jeikeium</i>	Yes	Negative	Yes	Survive
Guerrero [24]	2013	78; M	PPM; no	<i>C striatum</i>	No	Vegetation on the CIED lead from the tricuspid valve to the right ventricular wall	Yes	Survive
Helbig [25]	2013	77; M	ICD; no	<i>C striatum</i>	No	Vegetation on the tip of CIED atrial lead at the interatrial level	Yes	Survive
Kaya [26]	2016	68; F	ICD; no	<i>C mucifaciens</i>	No	Vegetation on the tip of CIED atrial lead and at the ostium of the superior vena cava	Yes	Not reported
Szymanska [27]	2019	79; F	PPM; not reported	<i>C striatum</i>	Yes	Negative	Yes	Survive
Pinto [28]	2021	48; M	CRT; no	<i>C striatum</i>	Yes	Tricuspid valve vegetation and CIED lead vegetation	Yes	Survive
Bulovic [29]	2022	82; M	PPM; no	Not reported	Yes	Mitral valve vegetation	Not reported	Not reported
Melo [30]	2022	73; F	PPM; no	<i>C striatum</i>	Yes	Small vegetation in the pacemaker lead	Yes	Survive
Anantharamakrishnan [31]	2023	70; F	PPM; no	<i>C striatum</i>	Yes	Tricuspid, mitral, and CIED vegetations	No	Death
Diab [32]	2023	76; M	ICD; no	<i>C striatum</i>	Yes	Negative	Yes	Not reported

Abbreviations: BSI, bloodstream infection; CIED, cardiac implantable electronic device; CRT, cardiac resynchronization therapy; F, female; ICD, implantable cardioverter-defibrillator; M, male; PPM, permanent pacemaker; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

[14, 34]. Third, patients who underwent device extraction after a confirmed CIEDI generally experienced favorable outcomes in our cohort and prior reported cases.

Although the relationship between *Corynebacterium* species and CIEDI has been minimally explored due to its rarity, insights from studies of corynebacterial infective endocarditis (IE) can be instructive for CIEDI [35]. Recent data from the Swedish National Registry identified 30 cases of corynebacterial IE (0.6%) of 5275 IE episodes over a decade, thereby demonstrating similarities with our findings, especially among elderly patients with prosthetic cardiac valves [36]. However, the rarity of these infections still constrains the generalizability.

Despite *Corynebacterium* species being an uncommon pathogen for endovascular infections, echocardiography was frequently utilized at our institution. The prevalent use of echocardiography in our study may explain an early detection of CIEDI, while in previous case reports, more than half of CIEDIs were diagnosed after recurring episodes of BSI rather than the initial episode. This could suggest that investigations for CIEDI were not routinely performed during the first BSI episode. We do not advocate for echocardiographic screening in all patients with CIED and corynebacterial BSI; however, in cases of persistent corynebacterial BSI without a clear source—especially in elderly patients with a prosthetic cardiac valve—a more thorough investigation may be warranted with a multispecialty team evaluation for CIEDI. In contrast to the high rate of echocardiography, the utilization of PET/CT was low, as its role in this clinical scenario (BSI with this uncommon organism) remains undefined.

This study has several limitations. The small sample size precluded a comprehensive risk factor analysis for CIEDI or outcomes. Referral bias, due to complex cardiac issues, may have skewed results toward a higher rate of investigation and diagnosis, limiting generalizability. Additionally, many patients with unknown status due to rapid progression of disease reflect the poor baseline status and disease severity.

This study underscores the importance of a vigilant approach to corynebacterial BSIs in patients with CIED, particularly when presenting without a clear infection source and with prosthetic cardiac valves. While the rarity of *Corynebacterium* species as a pathogen in CIEDI presents challenges in clinical management, early and tailored investigations could lead to accurate diagnosis of CIEDI. Future multicenter studies are needed to refine treatment strategies of patients with CIED and atypical pathogen BSI.

Notes

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D. C. D.), (2) drafting of the manuscript or revising it critically for important intellectual content (S. C., L. M. B., M. R. S., B. R. P., M. M., H. T., M. T. M., M. F., D. W. C., D. C. D.), and (3) final approval of the manuscript submitted (S. C., L. M. B., M. R. S., B. R. P., M. M., H. T., M. T. M., M. F., D. W. C., D. C. D.).

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