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Early Versus Delayed Lead Extraction in Patients With Infected Cardiovascular Implantable Electronic Devices

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ABSTRACT

OBJECTIVES This study sought to assess the impact of early versus delayed lead extraction in patients with an infected cardiovascular implantable electronic device (CIED).

BACKGROUND CIED infections are associated with poor outcomes. Prior studies have demonstrated improved survival with CIED extraction compared with antibiotic therapy alone. The impact of timing of CIED extraction has not been well characterized.

METHODS All infected CIED extraction cases at our medical center from 2006 to 2019 were reviewed. Patients were divided into 2 groups based on the presence of bacteremia or isolated pocket infection. We assessed the in-hospital morbidity and 1-year mortality for early versus delayed lead extraction, using hospitalization day 7 as cutoff.

RESULTS Of 233 patients who underwent CIED extraction, 127 patients had bacteremia and 106 patients had pocket infection. Delayed extraction (15.2 days) in bacteremic patients was associated with septic shock (odds ratio [OR]: 5.39; 95% confidence interval [CI]: 1.23 to 23.67; $p = 0.026$), acute kidney injury (OR: 5.61; 95% CI: 2.15 to 14.63; $p < 0.001$), respiratory failure (OR: 5.52; 95% CI: 1.25 to 24.41; $p = 0.024$), and decompensated heart failure (OR: 3.32; 95% CI: 1.10 to 10.05; $p = 0.033$). Locally infected patients with delayed extraction (10.7 days) were associated with acute kidney injury (OR: 3.45; 95% CI: 1.11 to 10.77; $p = 0.033$) and respiratory failure (OR: 10.29; 95% CI: 1.26 to 83.93; $p = 0.030$). Delayed CIED extraction in both groups was associated with increased 1-year mortality.

CONCLUSIONS Delayed infected CIED extraction is associated with worse outcomes. This underscores the importance of early detection and a strategy for prompt management including lead extraction.
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Cardiovascular implantable electronic devices (CIEDs) have become increasingly prevalent over the years as implantable cardioverter-defibrillators and permanent pacemakers have been shown to improve survival in patients with heart disease (1-4). Despite the use of antibiotics, recent studies suggest that the rate of CIED infections is on the rise (5-8). Many predictors for CIED infection have been reported, including various patient comorbidities (9,10) and procedure-related factors (9,11,12). CIED infections are associated with poor outcomes in morbidity and mortality (13,14).

Multiple studies have assessed the survival benefit of device removal in addition to antibiotic therapy in the management of CIED infections (15-18). Given the high rate of persistent or recurrent infection in patients treated with antibiotics alone, the 2017 Heart Rhythm Society expert consensus statement on CIED lead management and extraction recommends complete device and lead removal in patients with

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

CIED = cardiovascular implantable electronic device

OR = odds ratio

definite CIED infection (class I-B) (19). However, device removal is often delayed in favor of antibiotic therapy due to perceived risk of complications or lack of specialists or equipment to perform lead extractions. The impact of timing of lead extraction on patients with infected CIED with or without bacteremia has not been well characterized. The purpose of our study is to assess the effect of early versus delayed lead extraction on in-hospital morbidity and long-term mortality in patients presenting with infected CIEDs.

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METHODS

PATIENT SELECTION AND STUDY DESIGN. This retrospective study consisted of 233 consecutive patients who underwent CIED lead extraction for the indication of infection from September 2006 to September 2019 at our medical center. Institutional Review Board approval was obtained prior to data collection. Patients were separately analyzed based on presence of bacteremia or isolated pocket infection. Bacteremia was defined as bacterial growth from consecutive blood cultures that were thought not to be contamination by the treating physicians. Isolated pocket infection was characterized by a combination of erythema, swelling, drainage, or erosion of the skin overlying the device without the presence of bacteremia. Within the 2 cohorts, patients were further divided into 2 groups based on time from hospital admission to CIED extraction (early vs. delayed group), using 7 days as the cutoff. We compared the in-hospital prevalence of septic shock, acute kidney injury, septic emboli, respiratory failure, decompensated heart failure, and hospital length of stay after CIED extraction. We also compared the 1-year mortality between early and delayed groups. Patients with <1 year of follow-up or who received continuity of care at their referring regional hospitals were excluded from this analysis.

STATISTICAL ANALYSIS. Categorical variables are presented as numbers with proportions and compared using chi-square test. Continuous variables are presented as mean ± SD and compared with the Student's *t*-test. In-hospital complication was compared using Firth logistic regression. Variables (heart failure, hypertension, chronic kidney disease, chronic lung disease, diabetes, age) were screened using univariate analysis and adjusted if $p < 0.20$. Kaplan-Meier estimate of 1-year mortality was performed and compared for all groups using the log-rank test. Statistical analysis was performed using SPSS for Windows version 26 (IBM Corporation, Armonk, New York). For all analyses, $p < 0.05$ (2-tailed) was considered statistically significant.

RESULTS

PATIENT POPULATION. Of a total of 233 patients who underwent infected CIED extraction, 127 had bacteremia and 106 had isolated pocket infection. Demographics and clinical characteristics of all patients are summarized in **Table 1**. Of the 127 patients with bacteremia, 33 underwent early extraction and 94 underwent delayed extraction (5.4 ± 1.7 days vs. 15.2 ± 7.2 days). More patients in the delayed extraction group were transferred to our medical center for lead extraction from a regional hospital (58% vs. 73%; $p = 0.09$). Although this did not reach statistical significance, patients in the delayed group were transferred to our medical center at a later time after initial presentation (4.3 ± 1.5 days vs. 11.9 ± 7.1 days; $p < 0.01$). Other notable differences between the early and delayed extraction groups included more heart failure (52% vs. 72%; $p = 0.029$), hypertension (58% vs. 78%; $p = 0.026$), chronic obstructive pulmonary disease (15% vs. 35%; $p = 0.031$), diabetes (27% vs. 53%; $p = 0.01$), lower hemoglobin (9.8 ± 2.0 vs. 11.4 ± 3.8 g/dL; $p < 0.01$), and higher international normalized ratio (1.4 ± 0.4 vs. 1.2 ± 0.2; $p < 0.01$) in the delayed group.

Of the 106 patients with isolated pocket infection, 90 underwent early extraction and 16 underwent delayed extraction (2.6 ± 2.4 days vs. 10.7 ± 3.5 days). More patients from the delayed group were referred from regional hospitals (51% vs. 94%; $p < 0.01$) and were transferred to our medical center at a later time after initial presentation (2.8 ± 1.1 days vs. 7.0 ± 2.9 days; $p < 0.01$). Other clinical characteristics were similar, except that the early extraction group had a lower creatinine level (1.1 ± 0.7 vs. 1.9 ± 2.5; $p = 0.017$).

MICROBIOLOGY. *Staphylococcus aureus* (62%) was the most prevalent organism isolated in the bacteremic group, followed by *Enterococcus faecalis* (11%), coagulase-negative staphylococci (8%), and streptococcal species (6%) (**Figure 1A**). Six bacteremic patients (5%) had polymicrobial infection, all in the delayed extraction group. In the isolated pocket infection group, coagulase-negative *Staphylococcus* was the most commonly isolated organism (25%), followed by *S. aureus* (22%), gram-negative rods (6%), *Enterobacter* species (4%), and fungi (4%) (**Figure 1B**). In total, 20 (9%) patients were culture negative, and culture data were not available for 13 (6%) patients, all in the isolated pocket infection group. Other less

TABLE 1 Patient Demographics

	Bacteremia			Local Infection		
	Early (n = 33)	Delayed (n = 94)	p Value	Early (n = 90)	Delayed (n = 16)	p Value
Age, yrs	64.9 ± 14.1	65.0 ± 12.9	0.978	69.0 ± 15.5	63.5 ± 16.9	0.202
Male	23 (69)	71 (76)	0.511	77 (86)	14 (88)	0.837
Ethnicity			0.284			0.638
White	21 (64)	59 (63)		58 (64)	10 (63)	
Black	5 (15)	14 (15)		7 (8)	0 (0)	
Other	7 (21)	21 (22)		25 (28)	6 (37)	
BMI, kg/m^2	28.9 ± 8.9	28.5 ± 6.0	0.308	26.8 ± 5.3	28.7 ± 9.6	0.276
Days to extraction	5.4 ±1.7	15.2 ± 7.2	<0.01	2.6 ± 2.5	10.7 ± 3.6	<0.01
Referred from OSH	19 (58)	69 (73)	0.09	46 (51)	15 (94)	<0.01
Days to transfer	4.3 ±1.5	11.9 ± 7.1	<0.01	2.8 ± 1.1	7.0 ± 2.9	<0.01
Vegetation present						
Lead	9 (27)	32 (34)	0.474	10 (11)	2 (13)	0.872
Valvular	4 (12)	16 (17)	0.506	14 (16)	1 (6)	0.325
Ejection fraction, %	48.5 ± 19.7	43.7 ± 18.8	0.223	45.4 ± 16.7	47.6 ± 20.0	0.643
Leads extracted						
Total	77	234		223	49	
Per patient	2.3 ± 0.5	2.5 ± 0.9	0.357	2.5 ± 0.8	3.1 ± 1.2	0.022
Lead age, months	76.2 ± 60.6	89.6 ± 102.3	0.312	80.8 ± 74.2	90.4 ± 62.6	0.427
Lead type			0.099			0.409
ICD	15 (19)	68 (29)		63 (28)	11 (22)	
PPM	62 (81)	166 (71)		160 (72)	38 (78)	
Comorbidities						
Heart failure	17 (52)	68 (72)	0.029	55 (61)	8 (50)	0.404
CAD	12 (36)	37 (39)	0.761	32 (36)	5 (31)	0.739
Atrial fibrillation	15 (45)	47 (50)	0.653	41 (46)	9 (56)	0.430
Hypertension	19 (58)	73 (78)	0.026	59 (66)	10 (63)	0.813
COPD	5 (15)	33 (35)	0.031	13 (14)	5 (31)	0.099
Diabetes	9 (27)	50 (53)	0.010	24 (27)	8 (50)	0.061
ESRD	4 (12)	18 (19)	0.359	3 (3)	1 (6)	0.573
Prior cardiac surgery	6 (18)	34 (36)	0.056	28 (31)	4 (25)	0.624
Medications						
Aspirin	18 (55)	55 (59)	0.692	47 (52)	7 (44)	0.532
Oral anticoagulation	11 (33)	40 (43)	0.471	32 (36)	6 (38)	0.881
Lab values						
White blood cells, 1,000/mm^3	7.9 ± 4.1	9.9 ± 6.6	0.113	7.4 ± 3.5	7.6 ± 5.4	0.907
Hemoglobin, g/dl	11.4 ± 3.8	9.8 ± 2.0	0.003	12.4 ± 1.7	12.1 ± 2.8	0.637
Platelets, 1,000/mm^3	202.2 ± 87.0	249.0 ± 126.2	0.051	194.4 ± 61.7	193.1 ± 80.2	0.942
Creatinine, mg/dl	1.8 ± 2.2	2.0 ± 1.7	0.705	1.1 ± 0.7	1.9 ± 2.5	0.017
INR	1.2 ± 0.2	1.4 ± 0.4	0.009	1.3 ± 0.4	1.3 ± 0.3	0.894
C-reactive protein, mg/dl	13.8 ± 8.1	12.7 ± 10	0.712	3.8 ± 4.6	5.3 ± 2.6	0.406

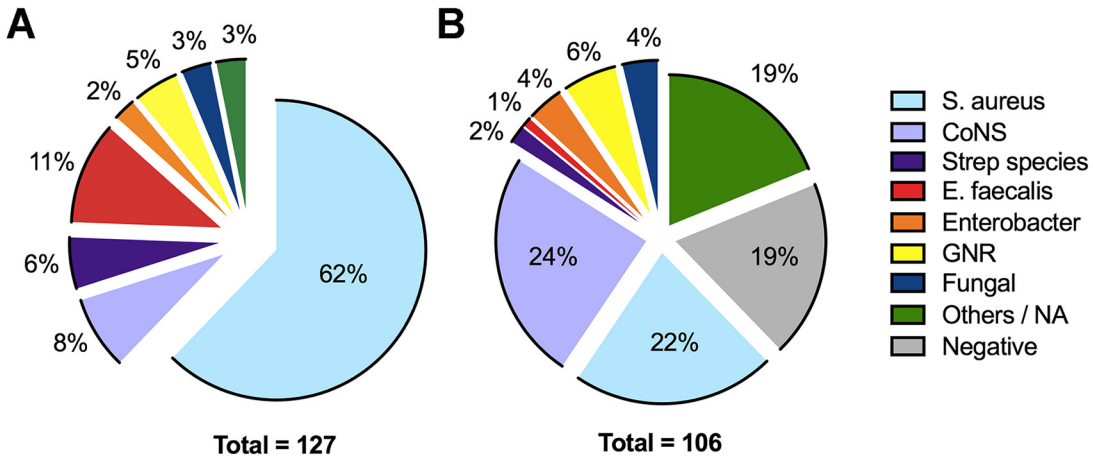
Values are mean ± SD, n (%), or n.

BMI = body mass index; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; ESRD = end-stage renal disease; ICD = implantable cardioverter-defibrillator; INR = international normalized ratio; OSH = outside hospital; PPM = permanent pacemaker.

commonly implicated organisms include *Propionibacterium acnes*, *S. hominis*, and *Corynebacterium jeikeium*.

CLINICAL OUTCOMES OF EARLY VERSUS DELAYED CIED EXTRACTION. Our results showed that delayed CIED extraction is associated with worse morbidity and mortality. In patients with bacteremia, 11 patients in the delayed extraction group died during the hospitalization compared with none in the early group (12% vs. 0%; p = 0.04). Cause of death included septic shock leading to multiorgan failure (n = 8), pulseless electrical activity arrest (n = 2), and anoxic brain injury secondary to massive hemorrhage from right atrial tear (n = 1). On Firth regression analysis, delayed CIED extraction in patients with bacteremia was associated with increased septic shock (odds ratio [OR]: 5.39; 95% confidence interval [CI]: 1.23 to 23.67; p = 0.026), acute kidney injury (OR: 5.61; 95% CI: 2.15 to 14.63; p < 0.001), respiratory failure (OR: 5.52; 95% CI: 1.25 to 24.41; p = 0.024), and

FIGURE 1 Microbiology of Infected Cardiovascular Implantable Electronic Devices



Organisms isolated from patients with **(A)** bacteremia and **(B)** isolated pocket infection. CoNS = coagulase-negative *Staphylococcus*; GNR = gram-negative rod; NA = not available.

decompensated heart failure (OR: 3.32; 95% CI: 1.10 to 10.05; p = 0.033) (Table 2). The delayed extraction group also had increased total antibiotic use (53.2 ± 13.7 days vs. 45.8 ± 16.7 days; p < 0.01).

In patients with isolated pocket infection, 1 patient in the delayed extraction group died of cardiac arrest compared with none in the early extraction group (6% vs. 0%; p = 0.017). On Firth regression analysis, the delayed extraction group had increased acute kidney injury (OR: 3.45; 95% CI: 1.11 to 10.77; p = 0.033) and respiratory failure (OR: 10.29; 95% CI: 1.26 to 83.93; p = 0.030) (Table 3). The delayed extraction group also had longer hospital stay after CIED extraction (11.1 ± 10.6 days vs. 7.8 ± 5.1 days; p = 0.043) and increased total antibiotic use (30.5 ± 10.7 days vs. 22.4 ± 11.8 days; p < 0.01). There was no difference in septic shock and decompensated heart failure.

One-year follow-up data were available for 178 of the 233 patients who underwent CIED extraction at our medical center. The Kaplan-Meier curve of 1-year mortality is shown in the Central Illustration. Patients who had delayed CIED extraction had higher mortality compared to those with early extraction in both the bacteremic infection group (log-rank p = 0.022) and isolated pocket infection group (log-rank p = 0.027).

PROCEDURAL OUTCOMES. A total of 592 leads were extracted in 233 patients with infected CIED. All leads were extracted using either manual traction, laser sheath, mechanical dilator, or open thoracotomy (Table 4). Of 233 patients, complete device and lead removal was successful in 223 patients. There were no differences in procedure duration (74.6 ± 35.7 min vs. 94.0 ± 66.0 min; p = 0.705) and fluoroscopy time (14.4 ± 17.6 min vs. 13.2 ± 13.5 min; p = 0.470) between early and delayed extraction in patients with bacteremia. Similarly, we did not observe differences in procedure duration (93.6 ± 42.8 min vs. 141.2 ± 105.1 min; p = 0.068) or fluoroscopy time (12.8 ± 9.9 min vs. 17.9 ± 13.6 min; p = 0.120) in patients with isolated pocket infection.

The overall major complication rate was 3%, with no statistically significant differences between the subgroups (Table 4). In patients with bacteremia who underwent early extraction, 1 patient developed a pocket hematoma while another patient had pericardial effusion that did not require surgical intervention. In patients with delayed extraction, procedural complications included pocket hematoma (n = 1) cardiac or vascular avulsion requiring surgical repair (n = 4), right ventricular lead fracture embolizing to the pulmonary artery (n = 1), and complete heart block followed by pulseless electrical activity arrest requiring brief cardiopulmonary resuscitation (n = 1). In patients with isolated pocket infection who had early extraction, complications included pocket hematoma (n = 1), cardiac or vascular avulsion requiring surgical intervention (n = 2), and tricuspid valve injury (n = 1). One patient in the delayed extraction group experienced vascular avulsion requiring surgical intervention.

DISCUSSION

Technological improvements in CIED extraction has made complete device removal in addition to antibiotic therapy the standard of care in patients with infected CIEDs (20). However, the impact of timing of device extraction on short- and long-term morbidity and mortality has not been well characterized. We report 3 main findings in our present study. First, delayed CIED extraction in bacteremic patients is associated with increased rates of septic shock, acute kidney injury, respiratory failure, and decompensated heart failure. Second, delayed CIED extraction in patients with isolated pocket infection is associated with acute kidney injury and respiratory failure. Third, delayed CIED extraction is associated with higher 1-year mortality in patients with bacteremia and isolated pocket infection.

INCREASING INCIDENCE OF CIED INFECTION. The incidence of CIED infection has increased significantly over the past few decades (7,8). This is partly contributed by the expanded indications for CIED implantation and also aging of the population requiring device upgrades and generator changes. In a meta-analysis by Polyzos et al. (9), device replacement or revision (OR: 1.98; 95% CI: 1.46 to 2.70) and generator change (OR: 1.74; 95% CI: 1.22 to 2.49) were associated with subsequent device infection. In a more recent study, the 15-year cumulative probability of CIED infection after the first, second, and third device manipulation was noted to be 2.6%, 2.7%, and 24.1%, respectively (5). Given the increasing incidence of CIED infections, it is important to expand the literature on patient outcomes in relation to timing of CIED extraction.

MICROBIOLOGY OF INFECTED CIEDs. Similar to prior studies (21–23), *S. aureus* and coagulase-negative *Staphylococcus* were the predominant implicated bacteria in our patient cohort for both bacteremia and isolated pocket infection. It is interesting to note that 19% of patients with isolated pocket infection had negative cultures. The incidence of culture-negative CIED infections has increased over the years, which could be reflective of the widespread use of oral antibiotics (21,24). Importantly, the failure of antibiotics for infected CIEDs in these cases highlight the necessity for CIED removal.

DELAYED CIED EXTRACTION IS ASSOCIATED WITH INCREASED MORBIDITY AND MORTALITY. A significant portion of patients was referred to our medical center from regional hospitals after a prolonged stay. This is similar to a prior study that noted 62% of patients transferred from regional hospitals, where they were given a variety of antimicrobials for a median of 10 days prior to transfer (16). This high rate of referral is not unexpected, as CIED extraction requires physician expertise and specialized equipment often available only at tertiary centers. It is interesting to note that patients with bacteremia underwent lead extraction at a much later time than those with pocket infections. This is consistent with a study by Viganego et al. (15), who reported lead extraction was performed 7.6 days after admission in patients with bacteremia compared with 1.3 days in those with pocket infections. This is likely contributed by the longer time required to establish a diagnosis of endovascular infection, which involves obtaining blood cultures and, in most cases, scheduling transesophageal echocardiography to assess for valvular or lead associated vegetations. In contrast, pocket infections are more readily diagnosed based on clinical presentation, usually manifesting as pocket site swelling, erythema, tenderness, purulent drainage, or device exposure.

Delayed extraction of infected CIEDs has been associated with worse outcomes. In a single-center, retrospective study involving 416 patients with mixed bacteremia and isolated pocket infection, immediate device extraction was associated with a 3-fold decrease in 1-year mortality when compared

TABLE 2 Clinical Outcomes of Patients With Bacteremia

	Bacteremia			
	Early (n = 33)	Delayed (n = 94)	Odds Ratio (95% CI)	p Value
Septic shock	2 (6)	25 (27)	5.39 (1.23–23.67)	0.026
Acute kidney injury	6 (18)	56 (62)	5.61 (2.15–14.63)	<0.001
Septic embolism	6 (18)	15 (17)	1.20 (0.41–3.50)	0.993
Respiratory failure	2 (6)	23 (26)	5.52 (1.25–24.41)	0.024
Decompensated HF	4 (12)	35 (39)	3.32 (1.10–10.05)	0.033

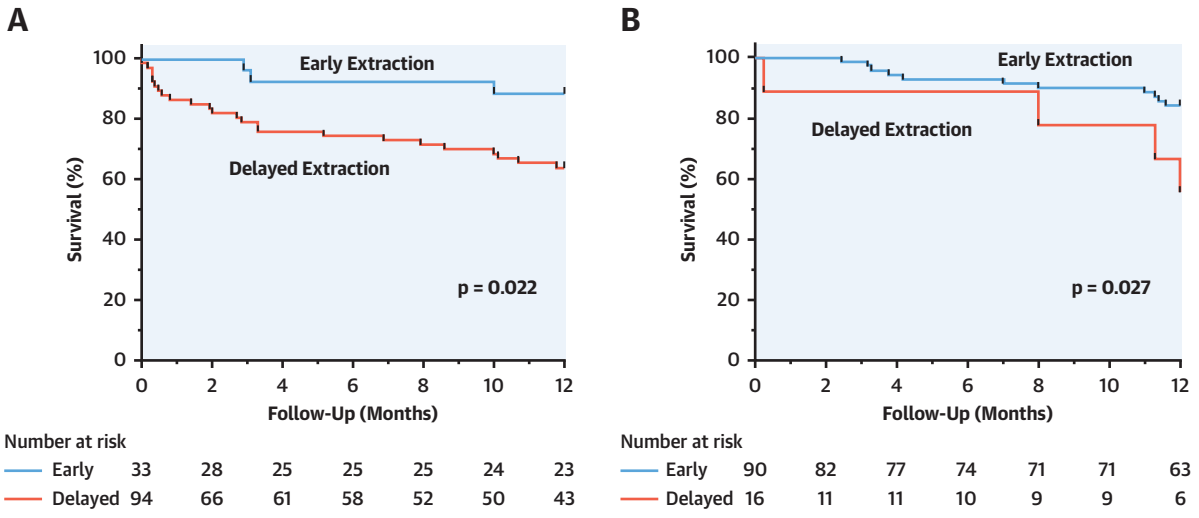
Values are n (%).
CI = confidence interval; HF = heart failure.

TABLE 3 Clinical Outcomes of Patients With Isolated Pocket Infection

	Local Infection			
	Early (n = 90)	Delayed (n = 16)	Odds Ratio (95% CI)	p Value
Septic shock	1 (1)	0 (0)	1.81 (0.07–46.34)	0.720
Acute kidney injury	18 (20)	7 (44)	3.45 (1.11–10.77)	0.033
Respiratory failure	1 (1)	2 (13)	10.29 (1.26–83.93)	0.030
Decompensated HF	15 (17)	3 (19)	1.42 (0.34–5.95)	0.631

Values are n (%).
Abbreviations as in Table 2.

CENTRAL ILLUSTRATION **Kaplan-Meier 1-Year Survival of Patients Undergoing Early Versus Delayed Cardiovascular Implantable Electronic Device Extraction**



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Patients with **(A)** bacteremia and **(B)** isolated pocket infection. Patients with delayed cardiovascular implantable electronic device extraction have lower survival rate at 1 year.

with delayed extraction and conservative therapy with antibiotics alone (16). Consistent with this study, we observed in our patient cohort that delayed CIED extraction was associated with a higher 1-year mortality and in-hospital morbidity, especially in patients with systemic infection. Contrary to the aforementioned study, we did not include patients who were treated with antibiotics without device removal, which has been shown to have worse outcomes, and we separately analyzed patients with bacteremia and isolated pocket infection. In another single-center, retrospective study involving 52 patients, a trend in higher in-hospital mortality was observed in patients who underwent lead extraction later during their hospitalization (15). The lack of statistical significance in this study is likely contributed by the small sample size and lack of multivariable analysis.

A retrospective study by Viganego et al. (15) reported the average hospitalization day to CIED extraction in patients with bacteremia was 7.6 days. According to the 2017 Heart Rhythm Society expert consensus document, the evaluation of patients with suspected infection begins with infectious disease consultation and blood cultures, which we allow 48 h to finalize. It is common practice to perform a transthoracic echocardiogram, followed by a transesophageal echocardiogram to evaluate the presence of valvular or lead vegetations, both of which require advanced scheduling and subject to potential delay. Time is also required to arrange the logistics of hospital transfer and the procedure is dependent on operating room availability. As such, we believe 7 days is a reasonable cutoff time between early and delayed extraction for this study, and a feasible goal for patients who are initially admitted to regional hospitals. Viganego et al. (15) reported a mortality benefit when CIED extraction occurred within 3 hospitalization days. Hence, an earlier cutoff could be considered for future prospective evaluation.

Although it is reasonable to think the presence of infectious complications may delay extraction procedures, it is important to emphasize that the decision on timing of lead extraction at our medical center is an individualized approach and based on a multidisciplinary evaluation involving an electrophysiologist, cardiothoracic surgeon, cardiac anesthesiologist, and nursing support for administration of complex medications (25). Hence, critically ill status does not preclude CIED extraction if clinically indicated. In fact, the importance of early source

TABLE 4 Procedural Characteristics

	Bacteremia			Local Infection		
	Early (n = 33)	Delayed (n = 94)	p Value	Early (n = 90)	Delayed (n = 16)	p Value
Major complications	0 (0)	5 (5)	0.594	2 (2)	1 (6)	0.756
Vascular avulsion	–	4		2	1	
PEA arrest	–	1		–	–	
Death	–	–		–	–	
Minor complication	2 (6)	2 (2)		2 (2)	0 (0)	
Pocket hematoma	1	1		1	–	
Pericardial effusion	1	–		–	–	
Lead embolization	–	1		–	–	
Tricuspid valve injury	–	–		1	–	
Procedure duration, min	74.6 ± 35.7	94.0 ± 66.0	0.705	93.6 ± 42.8	141.2 ± 105.1	0.065
Fluoroscopy time, min	14.4 ± 17.6	13.2 ± 13.5	0.470	12.8 ± 9.9	17.9 ± 13.6	0.120
Complete procedure success	31 (94)	90 (96)	0.435	86 (96)	16 (100)	0.668
Method of extraction			0.321			0.502
Manual traction	9 (27)	22 (23)		13 (14)	2 (13)	
Laser sheath	18 (55)	50 (54)		67 (75)	10 (63)	
Mechanical	6 (18)	18 (19)		8 (9)	3 (18)	
Thoracotomy	0 (0)	4 (4)		2 (2)	1 (6)	

Values are n (%), n, or mean ± SD. Procedure duration was defined as time of incision to time of closure.
PEA = pulseless electrical activity.

control in sepsis in improving outcomes is well established in medical literature (26,27). Consistent with this concept, the British guideline recommends urgent referral to extraction centers for patients with infected devices (28). Our findings add to the literature and highlight the importance of early source control in preventing sequelae of infection and sepsis in patients with infected CIEDs.

PROCEDURAL COMPLICATION DURING EXTRACTION OF INFECTED CIEDs. CIED infection is known to be associated with increased risk of procedural complication, though no significant difference was observed between early and delayed extraction. Sood et al. (29) reviewed data from the National Cardiovascular Data Registry Implantable Cardioverter-Defibrillator Registry involving 11,304 extraction procedures across 762 centers, CIED infection was associated with increased major perioperative complication, with an OR of 2.27 (95% CI: 1.70 to 3.04; $p < 0.0001$). Similarly, Hosseini et al. (30) reviewed the outcomes of 59,082 patients who underwent lead extraction of infected CIEDs from the National Inpatient Sample database and found that 10.4% of patients had at least 1 periprocedural complication. Seven (3%) patients in our study had cardiac or vascular avulsion, which is comparable to other studies that assessed outcomes of extractions of infected CIEDs (15,16). It is important to note that patients who experienced avulsion in our study had significantly older leads compared with those who did not (135.2 months vs. 78.4 months; $p < 0.01$), a risk factor known to be associated with procedural complications. Despite the procedural risks, extraction of infected CIEDs is associated with better long-term outcome and remains the standard of care.

STUDY LIMITATIONS. Our study is limited by the inherent nature of retrospective designs. First, a significant portion of our patients who underwent delayed extraction were referred to our medical center from regional hospitals. We were unable to delineate the cause for delay in transfer, but we suspect most cases were related to time required for work-up of endovascular infection and the logistics of coordinating hospital transfer. Second, treatment decisions including antimicrobial selection and decision to proceed with lead extraction were not standardized, but rather were determined on a case-by-case basis by the primary cardiologist in consultation with the infectious disease team. Third, patients who were transferred back to referring hospitals prior to the completion of their index hospitalization were excluded from our analysis due to lack of follow-up data, potentially introducing selection bias for a more complex patient cohort. Last, although we observed higher 1-year mortality in bacteremic patients with delayed extraction, they did have a

higher proportion of certain comorbidities, which could potentially confound the results. However, our findings were still consistent with prior studies. Despite these limitations, we believe that prompt diagnostic work-up and early source control with device extraction are imperative in the management of CIED infections.

CONCLUSIONS

Delayed infected CIED extraction is associated with worse in-hospital morbidity and higher rates of 1-year mortality in patients with bacteremia and isolated pocket infection. This underscores the importance of early detection of CIED infection and a strategy for prompt management including lead extraction.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In a comparison of patients with infected CIEDs who underwent device removal, this study showed that early extraction is associated with decreased in-hospital morbidity in patients with bacteremia and isolated pocket infection. Furthermore, the benefit of early extraction for infected CIEDs extends long term, as these patients demonstrated lower mortality rates at 1-year follow-up. These findings indicate prompt diagnostic work-up and early source control with device extraction are imperative in the management of CIED infections.

TRANSLATIONAL OUTLOOK: Perceived risk of procedural complications and lack of specialists have historically limited the performance of lead extractions. However, such procedures are now routinely performed at tertiary medical centers due to improvement in extraction technique and growing physician expertise. Although prior works have shown benefits of lead extraction over antibiotic therapy alone for CIED infections, this study further demonstrates the impact of early device extraction on improving patient outcomes and highlights the importance of a strong referral system between regional hospitals and tertiary medical centers.

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KEY WORDS **cardiovascular implantable electronic device, CIED infection, implantable cardioverter-defibrillator, lead extraction, permanent pacemaker**