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Clinical Presentation and Outcomes of Cardiovascular Implantable Electronic Device Infections in Hemodialysis Patients

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Abstract

Background—Infection is a serious complication of cardiovascular implantable electronic device (CIED) implantation. Kidney failure is as an independent risk factor for CIED infection and associated mortality. The presence of multiple comorbid conditions may contribute to varied clinical presentations and poor outcomes in hemodialysis (HD)–dependent patients with cardiac device infection.

Study Design—Case series.

Setting & Participants—CIED infections in HD patients (n=17) and non-HD patients (n=398) at Mayo Clinic in Rochester, MN, between 1991 and 2008.

Outcomes—Surgical management and death.

Measurements—Clinical presentations, microbial organisms.

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Results—Of the 415 patients admitted with CIED infection, 17 (4%) were receiving long-term HD therapy. Among those on HD, mean age was 72±15 (SD) years, 59% were female, and 53% had a central venous catheter for dialysis access. All 17 patients receiving HD therapy presented with CIED-associated bloodstream infection and 41% of these had infected vegetations on CIED leads or cardiac valves. A majority (82%) were managed with complete device removal and almost half (43%) received a replacement device once bloodstream infection cleared. Device infection was associated with significant short-term mortality in HD patients and 90-day survival was only 76% in this group of patients.

Limitations—Smaller sample size, majority white cohort, observational study.

Conclusions—CIED infection in patients receiving HD therapy is usually associated with bloodstream infection and is frequently complicated with device-related endocarditis. Despite complete device removal in the majority of HD patients with infection, mortality remains high.

Keywords

bacteremia; defibrillator; hemodialysis; pacemaker; mortality; cardiovascular implantable electronic device (CIED); end-stage renal disease (ESRD); bloodstream infection

By the end of December 2010, 593,086 patients were living with a diagnosis of end-stage renal disease (ESRD) in the United States and approximately 65% of them were receiving hemodialysis (HD) therapy¹. In this growing population, all-cause mortality is 6- to 8-fold higher compared to in the general population¹. Most of this excess mortality is attributed to the higher burden of cardiovascular diseases and infections. Sudden cardiac death accounts for the single largest cause of death in dialysis-dependent patients^{2,3}. Cardiovascular implantable electronic devices (CIEDs) are being increasingly used to minimize the risk of sudden death in this group⁴. An investigation by Herzog et al provided further credence to this approach by demonstrating that CIED implantation was independently associated with a 42% reduction in mortality in dialysis patients hospitalized for an index event of cardiac arrest⁵. Unfortunately, the rates of CIED-related infections are increasing more rapidly than the rates of device implantation⁶. These device infections not only mitigate some of the mortality benefits attributed to CIED therapy in HD patients but also associate with increased healthcare costs, prolonged hospital stays, and higher mortality rates among these individuals⁷.

A variety of factors contribute to the morbidity associated with CIED implantation in HD patients. A graded risk of bleeding and infection-related complications is associated with the degree of decreased kidney function, notably highest in those with ESRD^{6,8–10}. Moreover, the presence of central venous catheters (CVCs) in HD patients predisposes them to an increased risk of bacteremia episodes and subsequent risk of CIED infection⁹. The combination of uremic milieu, a high prevalence of indwelling CVCs, and chronic immune dysfunction associated with kidney failure likely contribute to the increased morbidity from CIED infection in individuals receiving HD^{1,9}. Severity of clinical presentation, complications associated with CIED infection, and surgical management of device infection in patients receiving HD therapy has not been previously addressed in the literature. The

objective of this retrospective study was to assess the distinctive features of CIED infection in HD-dependent patients.

Methods

Study Overview

The Mayo Clinic Heart Rhythm Device Database, surgical index and computerized central diagnostic index were reviewed to identify all cases of CIED infection between January 1, 1991, and December 31, 2008. All patients consented to the use of their medical records for research purposes. The Mayo Foundation Institutional Review Board approved the study.

Definitions

A CIED infection was classified as a pocket infection based on clinical presentation or positive microbial cultures from the device surface or pocket tissues with or without positive blood cultures as previously described by our group^{11–13}. A CIED-related bloodstream infection was defined as bacteremia in the absence of an alternative nidus of infection, and resolution of bloodstream infection after device explantation.

CIED-related infective endocarditis (CIED-IE) was defined using pathologic criteria for CIED lead or valve infection for patients who underwent surgical removal, or using a clinical criterion¹⁴ for patient who underwent percutaneous device removal. Clinically, patients were classified as having CIED-IE if they had positive echocardiographic findings and two or more positive blood cultures for typical skin organisms (coagulase-negative staphylococci [CoNS], *Corynebacterium* species, *Propionibacterium* species), or one positive blood culture for all other microorganisms. Positive echocardiographic findings for CIED-IE were defined as presence of an oscillating intracardiac mass on cardiac valve or supporting structures (in the path of regurgitant jets), or CIED leads in the absence of an alternative anatomic explanation, or visualization of a cardiac abscess, or new dehiscence of prosthetic valve¹⁰. The remaining patients were rejected as having CIED- IE.

Complications of extraction included damage to the tricuspid valve that required valve annuloplasty, subclavian vein laceration, hemothorax, pocket hematoma, fracture of lead tip requiring surgical intervention, hemorrhage that required surgical intervention, and postoperative cardiac arrest requiring intensive care unit stay. Patients receiving long-term HD therapy at the time of CIED infection were considered HD dependent. Patients without HD therapy at time of infection were identified as non-HD patients.

Patient Demographics and Device-Related Variables

Demographic variables included the patient's age, gender and race/ethnicity. Patients' medical records were reviewed for comorbid conditions, presenting systemic signs/symptoms, and laboratory parameters for potential predictors of mortality. Device characteristics included device type, number of leads, place of CIED implantation, indication for implantation, procedure type, anatomical site of implantation, and device age.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation or median (range). Categorical variables were described as count (percentage). Mortality rate was estimated using the Kaplan-Meier method and log rank tests were used for comparisons between survival curves for HD and non-HD patients. Proportional hazards regression (Cox) models were used to quantify the association of dialysis with the outcome of death. Event times were defined as the time elapsed from hospital admission to death. Subjects free of a death event were censored at last follow-up. Vital status and death dates, when available, were obtained from the US Social Security Index on December 1, 2010. Patients who were still alive according to this index were assumed to be alive as of June 1, 2010. P values < 0.05 were considered statistically significant and 95% confidence intervals (CIs) were reported. Statistical analyses were performed with JMP 9.0 (SAS Institute Inc, Cary, NC).

Results

Overall, there were 415 patients admitted to Mayo Clinic Rochester between 1991 and 2008 who met the criteria for CIED infection (Table 1). Among them, 17 (4%) were receiving long-term HD at the time of initial diagnosis. No patients were using home dialysis modalities such as peritoneal or HD therapy. Mean age, race, coronary artery disease and other comorbidities were similar between groups. There were more females in the HD group compared to the non-HD (59% vs. 24%, respectively). Over half (53%) of HD patients had a CVC in place at time of diagnosis.

Baseline features and complications of CIED infection are listed in Table 2. All HD patients presented with positive blood cultures. The majority (77%) had fever and leukocytosis (mean white blood cell count, 15 ± 9 [standard deviation] $\times 10^9/L$). In comparison, pocket infection was a more common presenting sign in non-HD patients. Patients in the HD group were more likely to have CIED-IE compared to those in the non-HD group (41% vs. 21%, respectively). The most common pathogens identified in HD patients were CoNS (29%), methicillin-resistant *Staphylococcus aureus* (MRSA) (29%), methicillin-susceptible *Staphylococcus aureus* (12%), and a variety of fungi (12%).

Surgical management of CIED infection for both HD and non-HD patients is summarized in Table 3. The majority (82%) of HD patients underwent device lead removal, among which less than half (43%) had a replacement device. Overall, the success rate of device removal and complications related to percutaneous extraction were similar between HD and non-HD patients.

Detailed clinical characteristics and outcomes of the 17 HD patients who were included in this case series are listed in Table 4. Thirteen (76%) received dialysis for 6 months or more prior to infection. None were treated with home dialysis therapies. The mean dialysis vintage was 82 (median, 28; range, 0.1–610) months. Nine patients (53%) utilized a CVC for dialysis access. All (100%) patients presented with blood stream infection. Seven (41%) had CIED-IE, of which 3 had an indwelling CVC. Devices were not removed in 3 of 17 patients due to an expectation of high operative risk and multiple comorbidities complicating the replacement of devices. Among those with device removal (n=14), 3 had

complications consisting of ventricular perforation, hematoma formation, and hypotension requiring pressors. At 90 days, 4 patients died, of which 3 had device extraction and complications during the procedure. Among the 3 patients who were medically managed, 1 died during the 90 days of followup.

The mean duration of follow up was 2.2 ± 2.9 years for the entire group (1.4 ± 1.6 in HD vs. 2.2 ± 2.9 in non-HD). By study end, 140 patients died (10 HD, 130 non-HD). During early follow up, survival rate was similar at 30 and 60 days between groups. At 90 days, survival was lower among HD patients (76% vs. 92%, respectively; log-rank $p=0.02$), Figure 1.

Discussion

While the association between kidney failure, CIED infection risk and associated morbidity and mortality has been previously reported^{10,15} a comprehensive analysis of the clinical presentation, complications, surgical management, and outcome of CIED infections based on dialysis dependency has not been previously explored. Although HD patients made up a small proportion (4%) of individuals with CIED infection in our study cohort, the clinical presentation of these patients differed from that of the non-HD group, suggesting that a discerning approach to evaluating for CIED infection may be necessary in these two patient groups. In our study, HD patients consistently presented with systemic infection and bacteremia (100%) at the time of initial presentation. Moreover, fever (76%) and leukocytosis (mean white blood cell count, $15 \pm 9 \times 10^9/L$) were frequent in this group of patients. In contrast, localized pocket infection was common in non-HD patients. Having CIED-IE was more often a complication in the HD compared to the non-HD group (41% vs. 21%, respectively). Interestingly, management differences were also observed, with CIED removal and re-implantation occurring less often in the HD group. Overall, early mortality rates were similar in the two groups; however at 90-days following hospital admission, fewer HD patients were alive.

Based on the 2012 US Renal Data System report, from 1991 through 2010, approximately 12,984 unique dialysis patients received an implantable cardioverter defibrillator/cardiac resynchronization therapy defibrillator device, of which 3,191 received a cardiac resynchronization therapy defibrillator device. Unfortunately, the mortality rate in dialysis patients remains high following implantation of implantable cardioverter defibrillator/cardiac resynchronization therapy defibrillator devices. The 2-year mortality rate reaches 53% following placement for primary prevention and nearly 58% following implantation for secondary prevention in dialysis patients¹. In a recent meta-analysis, the risk of death observed in dialysis compared with non-dialysis CIED patients was 2.7-fold greater¹⁶. These results are discouraging but reflect the complex medical issues and unyielding morbidity faced by our dialysis population. Given supportive data that CIED implantation improves outcomes⁵, its use in dialysis patients will likely be maintained, hence CIED infection remains an important clinical issue for both patients and providers.

Understanding the clinical presentation and outcome of CIED infection in this unique group of patients is important in terms of both diagnostic and management considerations. In general, inflammatory changes at CIED generator pocket is the most frequent finding on

physical examination that alerts patients and clinicians to the possibility of underlying CIED infection¹⁷. However, HD patients were less likely to have this presentation in our case series. This may be partly due to the blunted immune system in individuals on HD that limits a localized reaction and places these patients at higher risk of systemic infection. Interestingly, bloodstream infection was present in all infected HD patients. Consequently, one may hypothesize that hematogenous seeding of device leads from others sources (CVC, for instance) of bloodstream infection may be the predominant mechanism for device infection in HD patients. Therefore, underlying CIED infection should be considered in the differential diagnosis of HD patients presenting with positive blood cultures. Of note, the absence of inflammatory changes at device pocket site should not dissuade clinicians from suspecting CIED infection in an HD patient.

Despite multiple quality improvement initiatives, infection remains the second most common cause of hospitalization and death in HD patients¹. The adjusted rate of hospital admissions in HD patients between 2009 and 2010 was 0.54 per patient-year for cardiovascular admissions followed closely by a rate of 0.47 per patient-year for infection related admissions¹. Hospitalization for bloodstream infection remains a major concern in the HD population. In our HD group, all 17 patients had bloodstream infection at time of CIED infection diagnosis and MRSA was identified as the causative pathogen in 29% of these patients. This is consistent with earlier observations from a British Renal Registry wherein the relative risk of MRSA bacteremia was several folds higher for dialysis patients compared to that for the general population¹⁸. In our study, CoNS and MRSA occurred at the same frequency in HD patients. The findings of CoNS bloodstream infection likely correlates with the significantly increased prevalence of CVCs as well as the frequent puncture of arteriovenous fistulas in HD patients allowing for subsequent contamination and seeding by skin flora organisms. Overall, *S. aureus* is implicated as the most common pathogen leading to bacteremia¹⁹ and endocarditis in dialysis patients²⁰. In our study cohort, of the 7 patients in the HD group who had CIED-IE, 3 cases were due to CoNS while methicillin-susceptible *Staphylococcus aureus*, MRSA, *Candida* species, and polymicrobial infection contributed to the remaining events. CIED-IE occurred in 4 patients with an arteriovenous fistula, of which 3 had CoNS bacteremia. In our group of HD patients, CIED-IE was distributed among those with and without a CVC. Therefore, absence of a CVC in an HD patient may not be used as exclusionary criteria to minimize the clinical suspicion of CIED infection and associated complications such as CIED-IE.

Earlier work by Kamalakannan and colleagues demonstrated that surgical intervention reduced mortality when compared to medical management in HD patients with valvular endocarditis²⁰. Immediate and complete device removal in patients presenting with CIED infection was associated with a 3-fold reduction in mortality in an earlier investigation from our institution.²¹ In general, complex surgical procedures may be delayed or even denied in the dialysis population due to the perception of increased risk of complications from multiple comorbidities and overall poor prognosis. These reasons were also prevalent in our study. In our current series, 95% of the non-HD patients and 82% of HD patients underwent device removal. Among those deemed suitable to undergo percutaneous device lead extraction, there was no significant increase in extraction-related complications in either

patient group. The impact of these differences in management interventions among HD patients requires further exploration in larger cohorts.

This study has certain limitations. First, the sample size of HD patients was quite small, which has limited our ability to detect independent relationships between clinically significant variables that differ between HD and non-HD populations. Second, the majority of the study cohort (95%) was white, limiting the generalizability of the results to other ethnic and racial groups. Third, our kidney failure group consisted of in-center HD patients and it is unclear what CIED infection risk remains in the peritoneal or home HD population. Finally, this is a case series, limiting the findings to associations instead of proving causality.

In conclusion, given the high frequency of sudden cardiac death in dialysis patients and proven improved outcomes with CIED placement, it is likely that subsequent CIED infections will remain an important complication faced by HD patients. Therefore, understanding the differences in clinical presentations of CIED infection in this population is critical and may allow for early and appropriate intervention. Finally, recognizing that risk of extraction-related complications in select HD patients with CIED infection is comparable to that in non-HD patients is important for developing future treatment protocols that minimize discrimination of care to this group of patients.

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References

1. USRDS 2012 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; Bethesda, MD: 2012.
2. Bleyer AJ, Russell GB, Satko SG. Sudden and cardiac death rates in hemodialysis patients. *Kidney Int. Apr; 1999* 55(4):1553–1559. [PubMed: 10201022]
3. Jadoul M, Thumma J, Fuller DS, et al. Modifiable practices associated with sudden death among hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study. *Clin J Am Soc Nephrol. May; 2012* 7(5):765–774. [PubMed: 22403271]
4. Charytan DM, Patrick AR, Liu J, et al. Trends in the use and outcomes of implantable cardioverter-defibrillators in patients undergoing dialysis in the United States. *Am J Kidney Dis. Sep; 2011* 58(3):409–417. [PubMed: 21664735]
5. Herzog CA, Li S, Weinhandl ED, Strief JW, Collins AJ, Gilbertson DT. Survival of dialysis patients after cardiac arrest and the impact of implantable cardioverter defibrillators. *Kidney Int. Aug; 2005* 68(2):818–825. [PubMed: 16014061]

6. Voigt A, Shalaby A, Saba S. Rising rates of cardiac rhythm management device infections in the United States: 1996 through 2003. *J Am Coll Cardiol.* Aug 1; 2006 48(3):590–591. [PubMed: 16875991]
7. Sohail MR, Henrikson CA, Braid-Forbes MJ, Forbes KF, Lerner DJ. Mortality and cost associated with cardiovascular implantable electronic device infections. *Arch Intern Med.* Nov 14; 2011 171(20):1821–1828. [PubMed: 21911623]
8. Tompkins C, McLean R, Cheng A, et al. End-stage renal disease predicts complications in pacemaker and ICD implants. *J Cardiovasc Electrophysiol.* Oct; 2011 22(10):1099–1104. [PubMed: 21489029]
9. Asif A, Salman L, Lopera G, Haqqie SS, Carrillo R. Transvenous cardiac implantable electronic devices and hemodialysis catheters: recommendations to curtail a potentially lethal combination. *Semin Dial.* Sep-Oct; 2012 25(5):582–586. [PubMed: 22353033]
10. Le KY, Sohail MR, Friedman PA, et al. Clinical Predictors of Cardiovascular Implantable Electronic Device-Related Infective Endocarditis. *Pace.* Apr; 2011 34(4):450–459. [PubMed: 21208230]
11. Sohail MR, Uslan DZ, Khan AH, et al. Management and outcome of permanent pacemaker and implantable cardioverter-defibrillator infections. *J Am Coll Cardiol.* May 8; 2007 49(18):1851–1859. [PubMed: 17481444]
12. Sohail MR, Uslan DZ, Khan AH, et al. Infective endocarditis complicating permanent pacemaker and implantable cardioverter-defibrillator infection. *Mayo Clin Proc.* Jan; 2008 83(1):46–53. [PubMed: 18174000]
13. Uslan DZ, Sohail MR, St Sauver JL, et al. Permanent pacemaker and implantable cardioverter defibrillator infection: a population-based study. *Arch Intern Med.* Apr 9; 2007 167(7):669–675. [PubMed: 17420425]
14. Greenspon AJ, Prutkin JM, Sohail MR, et al. Timing of the most recent device procedure influences the clinical outcome of lead-associated endocarditis results of the MEDIC (Multicenter Electrophysiologic Device Infection Cohort). *J Am Coll Cardiol.* Feb 14; 2012 59(7):681–687. [PubMed: 22322085]
15. Bloom H, Heeke B, Leon A, et al. Renal insufficiency and the risk of infection from pacemaker or defibrillator surgery. *Pacing Clin Electrophysiol.* Feb; 2006 29(2):142–145. [PubMed: 16492298]
16. Sakhuja R, Keebler M, Lai TS, McLaughlin Gavin C, Thakur R, Bhatt DL. Meta-analysis of mortality in dialysis patients with an implantable cardioverter defibrillator. *Am J Cardiol.* Mar 1; 2009 103(5):735–741. [PubMed: 19231344]
17. Dababneh AS, Sohail MR. Cardiovascular implantable electronic device infection: A stepwise approach to diagnosis and management. *Clev Clin J Med.* Aug; 2011 78(8):529–537.
18. Fluck R, Wilson J, Davies J, Blackburn R, O'Donoghue D, Tomson CR. UK Renal Registry 11th Annual Report (December 2008): Chapter 12 Epidemiology of Methicillin Resistant *Staphylococcus aureus* bacteraemia amongst patients receiving Renal Replacement Therapy in England in 2007. *Nephron Clin Pract.* 2009; 111(Suppl 1):c247–256. [PubMed: 19542700]
19. Chan KE, Warren HS, Thadhani RI, et al. Prevalence and outcomes of antimicrobial treatment for *Staphylococcus aureus* bacteremia in outpatients with ESRD. *J Am Soc Nephrol.* Sep; 2012 23(9): 1551–1559. [PubMed: 22904350]
20. Kamalakannan D, Pai RM, Johnson LB, Gardin JM, Saravolatz LD. Epidemiology and clinical outcomes of infective endocarditis in hemodialysis patients. *Ann Thorac Surg.* Jun; 2007 83(6): 2081–2086. [PubMed: 17532401]
21. Le KY, Sohail MR, Friedman PA, et al. Impact of timing of device removal on mortality in patients with cardiovascular implantable electronic device infections. *Heart Rhythm.* Nov; 2011 8(11):1678–1685. [PubMed: 21699855]

Figure 1.
90-day survival based on hemodialysis status in patients with CIED infections

Table 1

Comparison of baseline patient demographics, device-related features, and comorbidities in patients with CIED infection

	All (N=415)	HD (n=17)	Non-HD (n=398)
Age (y)	69 ±15 (72; 17–95)	72 ±15 (79; 41–92)	69 ±15 (72; 17–95)
Female sex	104 (25%)	10 (59%)	94 (24%)
White race	376 (91%)	16 (94%)	360 (90%)
Diabetes mellitus	115 (28%)	8 (47%)	107 (27%)
Coronary artery disease	237 (57%)	8 (47%)	229 (58%)
CABG	117 (28%)	3 (18%)	114 (29%)
Cirrhosis	4 (1%)	0 (0%)	4 (1%)
Malignancy	50 (12%)	1 (6%)	49 (12%)
Dementia	12 (3%)	0 (0%)	12 (3%)
COPD	67 (16%)	3 (18%)	64 (16%)
Immunosuppressive therapy	13 (3%)	0 (0%)	13 (3%)
Central venous catheter	27 (7%)	9 (53%)	18 (5%)
Vascular graft	9 (2%)	3 (18%)	6 (2%)
Ejection fraction (%)	43 ± 17 (45; 10–75); n=376	47 ± 14 (45; 20–74); n=17	43 ± 17 (45; 10–75); n=359
Type of device			
Permanent pacemaker	256 (62%)	8 (47%)	248 (62%)
ICD	159 (38%)	9 (53%)	150 (38%)
No. of chambers			
Single	89 (21%)	7 (41%)	82 (21%)
Dual	326 (79%)	10 (59%)	316 (79%)
Previous CIED infection	47 (11%)	2 (12)	45 (11)

Note: Values for categorical variables are given as number (percentage); values for continuous variables are given as mean ± standard deviation (median; range).

Abbreviations: CABG (coronary artery bypass grafting), COPD (Chronic obstructive pulmonary disease; CIED, cardiovascular implantable electronic device; HD, hemodialysis; ICD, Implantable cardioverter defibrillator

Table 2

Comparisons of baseline symptoms and microbiology in HD and Non-HD patients with CIED infection

	All (N=415)	HD (n=17)	Non-HD (n=398)
Onset of symptoms (d)	36 ±117	15 ±43	37 ±119
WBC count, (x10 ⁹ /L)	10±6	15±9	10±6
Hematocrit (%)	36±6	33±5	36±6
Serum creatinine (mg/dL)	1.5 ± 1.0 (1.2; 0.6–9.8)	4.8 ± 8 (4.7; 1.7–9.8)	1.4 ± 0.4 (1.2; 0.6–6.1)
eGFR* (ml/min/1.73 m ²)	58±25	13±3	60±60
ESR (mL/1 h)	37±30; n=152	69±91; n=5	36±6; n=147
C-reactive protein (mg/L)	29 ±51; n=34	20; n=1	29 ±9; n=33
Fever	168 (40%)	13 (77%)	155 (39%)
Hypotension [^]	46 (11%)	3 (17%)	43 (11%)
Tachycardia	33 (8%)	2 (12%)	31 (8%)
Erythema	209 (50%)	0	209 (53%)
Pain at pocket site	119 (29%)	1 (6%)	118 (30%)
Pocket swelling	188 (45%)	1 (6%)	187 (47%)
Tenderness	134 (32%)	1 (6%)	133 (33%)
Drainage from pocket	160 (39%)	0	160 (40%)
Purulent drainage	99 (24%)	0	99 (25%)
Skin ulcer	68 (16%)	0	68 (17%)
Skin erosion of lead/generator	93 (22%)	0	93 (23%)
Positive blood culture	192 (46%)	17 (100%)	175 (44%)
Endocarditis**	89 (21%)	7 (41%)	82 (21%)
Bacterial Organism			
CoNS	158 (38%)	5 (29%)	153 (38%)
MRSA	39 (9%)	5 (29%)	34 (9%)
MSSA	90 (22%)	2 (12%)	88 (22%)
<i>S viridans</i>	1 (0.2%)	0	1 (0.3%)
<i>Enterococcus</i>	17 (4%)	1 (6%)	16 (4%)
<i>E coli</i>	1 (0.2%)	0	1 (0.3%)
<i>Klebsiella</i>	2 (0.5%)	0	2 (0.5%)

	All (N=415)	HD (n=17)	Non-HD (n=398)
<i>Serratia</i>	5 (1%)	0	5 (1%)
<i>Pseudomonas aeruginosa</i>	5 (1%)	0	5 (1%)
<i>Corynebacterium</i> spp	4 (1 %)	0	4 (1%)
<i>Propionibacterium</i> spp	12 (3%)	0	12 (3%)
<i>S bovis</i>	1 (0.2%)	0	1 (0.3%)
βHS-Gp B	1 (0.2%)	0	1 (0.3%)
<i>Mycobacteria</i> spp	0	0	0
<i>Candida</i>	3 (0.7%)	1 (6%)	2 (0.5%)
Other fungal	3 (0.7%)	0	3 (0.8%)
Polymicrobial	32 (8%)	2 (12%)	30 (8%)
Gram positive, culture negative	4 (1%)	0	4 (1%)
Gram negative, culture negative	25 (6%)	0	25 (6%)
Other organism	12 (3%)	1 (6%)	11 (3%)
MRSA and MSSA	129 (31%)	7 (41%)	122 (31%)

Note: Values for categorical variables are given as number (percentage); values for continuous variables are given as mean ± standard deviation (median; range). Conversion factor for serum creatinine in mg/dL to μmol/L, ×88.4.

Abbreviations: CoNS: coagulase-negative Staphylococci, MRSA: methicillin-resistant *Staphylococcus aureus*, MSSA: methicillin-susceptible *Staphylococcus aureus*; WBC, white blood cell; ESR, erythrocyte sedimentation rate; CIED, cardiovascular implantable electronic device; HD, hemodialysis; βHS-Gp B, beta hemolytic streptococci-group B; eGFR, estimated glomerular filtration rate; *E coli*, *Escherichia coli*; *S bovis*, *Streptococcus bovis*; *S viridans*, *Staphylococcus viridans*.

* calculated using the *** equation.

** Endocarditis: CIED-related infective endocarditis.

^ Hypotension defined as systolic blood pressure <90 or diastolic blood pressure <60 mm Hg.

Table 3

Comparisons of treatment and relapse in patients with CIED infection

	All (N=415)	HD (n=17)	Non-HD (n=398)
Device removal	393 (95%)	14 (82%)	379 (95%)
Successful percutaneous extraction	337 (92%); n=365	14 (100%); n=14	323 (92%); n=351
Complications related to percutaneous extraction	41 (11%); n=365	3 (21%); n=14	38 (11%); n=351
New device placed	266 (68%); n=393	6 (43%); n=14	260 (67%); n=379
Relapse	15 (4%); n=387	1 (6%)	14 (4%)

CIED, cardiovascular implantable electronic device; HD, hemodialysis

Table 4

Baseline patient characteristics and outcomes in HD patients with CIED infection.

Patient No.	Age (y)	Sex	CIED Indication	Dialysis Vintage (mo)	Dialysis Access Type	Bacterial Organism	Endocarditis	CIED Removal	Removal Complication	Device Replaced	Death in 90 d
1	84	M	Heart block	24	AVF	CoNS	Yes	Yes	No	Yes	No
2	83	F	Syncope	28	AVF	Other	No	No	N/A	N/A	No
3	82	F	Sinus node	41	AVF	CoNS	Yes	Yes	No	No	No
4	73	F	V tach/fib	62	AVF	CoNS	Yes	Yes	No	No	No
5	61	M	V tach/fib	61.1	AVF	MSSA	No	Yes	Yes	No	Yes
6	56	M	V tach/fib	141	AVF	MSSA	Yes	Yes	Yes	Yes	Yes
7	47	F	Heart block	12	AVF	CoNS	No	No	N/A	N/A	No
8	79	F	Other	137	AVG	Polymicrobial	No	Yes	No	No	No
9	†90	F	Heart block	19	CVC	CoNS	No	Yes	No	Yes	No
10	84	M	SVT	17	CVC	MRSA	No	Yes	No	Yes	No
11	81	M	Heart block	0.6	CVC	MRSA	No	Yes	No	Yes	No
12	80	M	Sinus node	88	CVC	<i>Enterococcus</i>	No	Yes	No	No	No
13	79	F	Sinus node	0.9	CVC	MRSA	No	No	N/A	N/A	Yes
14	77	F	Sinus node	0.08	CVC	MRSA	Yes	Yes	No	No	No
15	66	F	Heart block	30	CVC	<i>Candida</i>	Yes	Yes	Yes	Yes	Yes
16	51	M	V tach/fib	4	CVC	MRSA	No	Yes	No	No	No
17	40	F	Other	182	CVC	Polymicrobial	Yes	Yes	No	No	No

AVF, arteriovenous fistula; AVG, arteriovenous graft; CoNS, coagulase-negative staphylococci; CVC, central venous catheter; CIED, cardiovascular implantable electronic device; HD, hemodialysis; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; N/A, not available; SVT, supraventricular tachycardia; V tach/fib, ventricular tachycardia/fibrillation