Cardiac implantable electronic device infection in patients with end-stage renal disease

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INTRODUCTION Cardiac implantable electronic devices (CIED) are increasingly being used in end-stage renal disease (ESRD) patients. These patients have a high risk of device infection.

OBJECTIVES To study the optimal management of device infections in patients with ESRD.

METHOD We used the United States Renal Data System (USRDS) to assess the presence of a CIED and associated comorbidities, risk factors for infection, and mortality following device extraction or medical management in ESRD patients with CIED infection. Univariable, multivariable, and survival analyses were performed using USRDS data from 2005 to 2009.

RESULTS Of 546,769 patients, 6.4% had CIED and 8.0% of those developed CIED infection. The major risk factors for device infection were black race, temporary dialysis catheter, and body mass index >25. Patients with artificial valves were excluded from the analysis. Only 28.4% of infected CIED were removed. CIED removal was more common in those with congestive heart failure. The median time to death following diagnosis of a CIED infection was 15.7 months versus 9.2 months for those treated via device extraction versus medical-only therapy (hazard ratio: 0.75; 95% confidence interval: 0.68–0.82).

CONCLUSION Patients with ESRD and infected CIEDs have a poor prognosis. Rates of device extraction are low, but this strategy appears to be associated with modest improvement in survival.

KEYWORDS Pacemaker; Implanted cardioverter-defibrillator; Infection; Device extraction

ABBREVIATIONS **aRR** = adjusted risk ratio; **CAD** = coronary artery disease; **CHF** = congestive heart failure; **CI** = confidence interval; **CIED** = cardiac implantable electronic devices; **ESRD** = end-stage renal disease; **HR** = crude hazard ratio; **LR** = likelihood ratio; **RR** = crude risk ratio; **USRDS** = United States Renal Data System

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Introduction

Cardiac implantable electronic devices (CIED) are increasingly used to treat bradyarrhythmias, tachyarrhythmias, and congestive heart failure (CHF).[1,2] Cardiovascular diseases, including arrhythmias and CHF, are the most common cause of death in patients with end-stage renal disease (ESRD).[3] Thus, ESRD patients frequently have indications for the use of CIED.

Infectious complications of CIED in the general population are relatively uncommon,[4] but are associated with significant morbidity and mortality.[5] The management of CIED infections usually includes the administration of antibiotics and removal of the infected hardware.[6] In the general population with an infected CIED, a survival advantage has been shown for patients treated with antibiotics and device extraction when compared to antibiotic therapy alone.[7]

ESRD patients are at increased risk of bloodstream infection owing to frequent vascular access for hemodialysis or indwelling catheters for temporary hemodialysis or for peritoneal dialysis.[8,9] Alterations in immune system function and limited inflammatory responses also put them at a higher risk for infection.[10] Current guidelines do not directly address the management of CIED infections in ESRD patients, since these patients have been excluded from nearly

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all clinical trials. To better understand current management practices and outcomes for ESRD patients with CIED infections, we queried the United States Renal Data System (USRDS). In this large cohort we assessed the prevalence of CIED use, risk factors for infection, and mortality following device extraction, or medical management without extraction, in patients with CIED infection.

Methods

Data source

The USRDS is a de-identified database that includes demographic characteristics, hospitalization and physician/supplier claims, and vital statistics on all ESRD patients in the United States.[8] We queried USRDS data from 2005 through 2009. Comorbidities were defined by ICD-9 billing codes submitted to Medicare. The latest version of the form CMS-2728 was used to obtain additional comorbidity information. CMS form 2728 is a medical information form used by Medicare to determine eligibility and is a required submission by dialysis units on every patient enrolled.

Outcome variables

There were 3 primary outcome variables in this study: 1) presence of a CIED, 2) CIED infection, and 3) medical versus device extraction and associated survival of an infected CIED (Supplemental Table 1).

Presence of a CIED

The presence of a CIED was defined a priori according to the following ICD-9 codes: V45.01 (cardiac pacemaker), V45.02 (automatic implantable cardiac defibrillator), 996.61 (infection and inflammatory reaction due to cardiac device, implant, and graft), or any CIED extraction code (Supplemental Table 2). Only diagnosis codes defining the presence of a CIED occurring on or after the date of the first ESRD service were included in the analysis. Patients with cardiac valve prostheses were excluded from the analysis.

CIED infection

This analysis was limited to those individuals with evidence of a CIED and the presence of a CIED infection based on ICD-9 code 996.61 (see above). Because this code may indicate either CIED infection or cardiac prosthetic valve endocarditis, patients with prosthetic valves were excluded. This code was considered valid only if it was present after the placement date of a CIED.

Medical treatment versus extraction of an infected CIED, and associated survival

Medical therapy of a CIED infection without hardware removal was inferred by the lack of surgical extraction codes. Device extraction was defined by the presence of at least 1 surgical extraction code (Supplemental Table 1). Surgical extraction codes were considered valid only if they were dated within the 60 days following the diagnosis of a CIED infection. Survival following medical therapy, or device extraction of an infected CIED, was assessed through December 31, 2011. Individuals who had not died during follow-up were also censored on this date. Among patients who died, the cause of death was classified as cardiac-related, infection-related, or other. Patients with cardiac valve prostheses were also excluded from this analysis.

Covariates

For all analyses, demographic characteristics considered included age at the onset of dialysis, sex, race/ethnicity, initial dialysis type, and year of first dialysis. Age was categorized as 18–39 years, 40–64 years, and greater than 65 years of age. Race was categorized as white, black, or other, or as Hispanic versus non-Hispanic. Demographic variables and date of first dialysis were obtained from the main USRDS patient database. The initial dialysis type was extracted from CMS-2728 version 2005, if available (25% of the study population had this available). For each set of analyses, covariates or potential risk factors as predictors of a given outcome of interest were considered, including several comorbid conditions as predictors for having a CIED or CIED infection. These variables differed in terms of data source and/or time of occurrence relative to the development of a CIED infection, and were divided into 3 general categories.

Category 1

Most comorbid conditions were identified based on the presence of 1 or more primary or secondary ICD-9 codes from hospitalization records that occurred from date of first ESRD service to date of the development of a CIED infection. Comorbid conditions considered specifically related to cardiovascular health were a history of atrial fibrillation or flutter, CHF, or coronary artery bypass graft. Other conditions reported were a history of cancer or sleep apnea. Comorbid conditions diagnosed prior to ESRD, and up to the diagnosis of a CIED infection, were included.

Category 2

For some comorbid conditions, we combined data from CMS-2728 with ICD-9 diagnosis codes to improve case finding. These comorbidities included a history of coronary artery disease (CAD), diabetes, hypertension, and alcohol use/abuse. These conditions may have occurred prior to ESRD or might have been a contributing factor to ESRD, and were included if they were present at or prior to the date of a CIED infection.

Category 3

Comorbid conditions considered as risk factors or conditions potentially requiring device extraction of an infected CIED included bacteremia, bacteremia with sepsis, infectious endocarditis, pulmonary embolism, and stroke. The presence of these conditions was inferred based on the presence of ICD-9 codes in the dataset within 2 days prior to and up to 7 days after the date of CIED infection.

Table 1 Characteristics of the study populations (%)

Variable	All patients	CIED present	CIED infection	Medical therapy	Device extraction
Total number*	546,769 (100.0)	34,935 (6.4)	2792 (0.5)	1999 (0.4)	793 (0.1)
Age, y (mean ± SD)	62.7 (15.4)	69.6 (12.1)	65.1 (13.5)	65.1 (13.8)	65.0 (12.8)
Female sex	239,945 (43.9)	13,544 (38.8)	1048 (37.5)	794 (39.7)	254 (32.0)
Race					
Black	156,259 (28.6)	8069 (23.1)	783 (28.0)	544 (27.2)	239 (30.1)
White	358,617 (65.6)	25,315 (72.5)	1913 (68.5)	1380 (69.0)	533 (67.2)
Initial dialysis access†					
Catheter	378,734 (68.9)	24,452 (70.0)	2165 (77.5)	1535 (76.8)	630 (79.5)
AV fistula	63,379 (11.6)	4032 (11.5)	231 (8.3)	165 (8.3)	66 (8.3)
AV graft	17,517 (3.2)	1253 (3.6)	64 (2.3)	45 (2.3)	19 (2.4)
"Other" access type	5623 (1.0)	387 (1.1)	36 (1.3)	23 (1.2)	13 (1.6)
Unknown	83,516 (15.3)	4811 (13.8)	296 (10.6)	231 (11.6)	65 (8.2)

AV = arteriovenous; CIED = cardiac implantable electronic device.

*Percentages for totals row are calculated out of total patients available for analysis (N = 546,769). All other percentages are calculated from column totals (eg, all in "CIED present" column are out of 34,935 individuals with a CIED).

†Derived from CMS form 2728 from 2005 and later. Previous versions (1990–2004) did not indicate the initial type of access.

Statistical Analysis

Descriptive statistics were calculated on all clinically relevant variables of interest. Frequency (percent) was reported for categorical variables, and the mean (standard deviation) or median (range) for continuous variables. Potential covariates of interest were stratified by presence of a CIED and bivariate analyses conducted (χ^2 or Wilcoxon rank sum tests). Bivariate general linear models were used to determine an association between outcomes and other factors of interest for presence of a CIED, CIED infection, or surgical extraction of a CIED. The analysis of the "surgical extraction of a CIED" cohort excluded those with an artificial heart valve. Multivariable general linear models were used to determine the relative contributions of potential predictors to the outcome of interest, based on significant associations found in bivariate analyses. Crude and adjusted relative risks (RR and aRR) were estimated using a log-binomial model. We used a modified Poisson regression method with robust error variance for instances when the log-binomial models would not converge.[11] Using backward elimination of nonsignificant variables, we obtained a final predictive model for each outcome of interest. RRs and 95% confidence intervals (CI) are reported. The final aRR was obtained after controlling for statistically significant confounders.

Survival analysis was used to determine if device extraction was a risk factor for all-cause mortality, measured in months for each person and independent of other potential predictors of death. We included only individuals with a CIED infection (excluding individuals with an artificial heart valve) and compared device extraction with presumed medical therapy. An unadjusted Cox proportional hazards regression model was used to evaluate the prediction of device extraction on survival. The period of interest for the device extraction model was calculated such that follow-up began at time of CIED infection and ended at death or the end of the follow-up period on December 31, 2011. Owing to the nature of the data, we assumed that censoring was noninformative and measurement error among the validated patient characteristics and ICD-9 diagnostic codes was relatively low. The crude and adjusted hazards ratio (HR, aHR) and 95% CI are reported.

Individuals were excluded from all analyses if they had any missing information for the main covariates of interest or had an ICD-9 code indicating a cardiac valve prostheses. Statistical analyses were performed using SAS v9.4 (SAS Institute, Cary, NC) and a type I error rate of 0.05. This study was reviewed by the Georgia Regents University Institutional Review Board and was determined to be non–human subject research because of the de-identified nature of the data and absence of qualifying protected health information.

Results

Characteristics of the study population

During the 5-year study period, 561,741 patients received their first ESRD-related service and 97.3% (546,769) met the study criteria. The majority of these individuals were male (56.1%), white (65.6%), and non-Hispanic (85.4%) (Table 1). The average age at first ESRD-related service was 62.7 years (standard deviation ±15.4 years). For those whose initial access type was known, catheter was the most common (68.9%).

Presence of a CIED and associated covariates

From the above cohort, 34,935 patients (6.4%) met the criteria for the presence of a CIED. Patients with CIED were more likely to be male, white, non-Hispanic, and older at the institution of dialysis than patients without a CIED (Table 1). Cardiovascular conditions were associated with increased likelihood of having a CIED, with likelihood ratio (LR)/aRR of 2.58 (95% CI 2.49–2.66) for CAD, 1.72 (95% CI 1.69–1.76) for atrial fibrillation, 3.62 (95% CI 3.50–3.74) for CHF, and 1.67 (95% CI 1.63–1.71) for coronary artery bypass graft (Table 2). The noncardiac conditions associated with the greatest likelihood of having a CIED were age ≥65 [LR/aRR 1.84 (1.70–1.98)], age 40–64 [LR/aRR 1.62 (1.22–1.42)], sleep apnea [LR/aRR 1.21 (1.16–1.26)], and diabetes [LR/aRR 1.05 (1.03–1.08)]. Women, black race, Hispanic

Table 2 Clinical characteristics of patients with a cardiac implantable electronic device

Risk factor	Adjusted RR	95% CI Lower	95% CI Upper
Sex: female vs male	0.82	0.80	0.84
Race: black vs white	0.96	0.94	0.99
Race: other vs white	0.99	0.94	1.04
Ethnicity: Hispanic vs non-Hispanic	0.90	0.87	0.93
Ethnicity: unknown ethnicity vs non-Hispanic	1.01	0.92	1.12
Age >65 years vs 18–39 years at ESRD diagnosis	1.84	1.70	1.98
Age 40–64 years vs 18–39 years at ESRD diagnosis	1.62	1.22	1.42
Access at first dialysis			
AV graft vs AV fistula	1.07	1.00	1.13
Dialysis catheter vs AV fistula	1.00	0.97	1.03
Other type vs AV fistula	0.97	0.88	1.07
Category 1 (cardiac) variables			
Congestive heart failure	3.62	3.05	3.74
Coronary artery bypass graft	1.67	1.63	1.71
Atrial fibrillation/flutter	1.72	1.69	1.76
Category 1 (noncardiac) variables			
Sleep apnea	1.21	1.16	1.26
Category 2 variables			
Coronary artery disease	2.58	2.49	2.66
Diabetes	1.05	1.03	1.08
Obesity (BMI >25)	1.06	1.04	1.08
Alcohol use/abuse	0.92	0.87	0.98
Hypertension	0.93	0.90	0.96

AV = arteriovenous; BMI = body mass index; ESRD = end-stage renal disease; RR = relative risk.

ethnicity, and alcohol use/abuse were associated with a decreased likelihood of CIED placement.

CIED infection and associated risk factors

In patients with a CIED, 8% met the criteria for an infected device (Table 1). Clinical risk factors with the greatest relative risk of a CIED infection included black race [aRR 1.08 (1.00–1.18)] and the use of a temporary dialysis catheter [aRR 1.56 (1.37–1.78)] or "other" type of access [aRR 1.61 (1.15–2.24)] (Table 3). No category 1 variables increased the risk of CIED infection; however, from the category 2 variables, a body mass index >25 significantly increased the risk of infection [aRR 1.13 (1.05–1.23)].

Medical treatment only versus device extraction and survival

Among patients with an infected CIED, 28.4% underwent device extraction. The likelihood of device extraction was increased in the presence of CHF (Table 4). Device extraction was less likely in the presence of bacteremia and stroke. No other variables were significant predictors of surgical extraction for an infected CIED.

During the 5-year follow-up period, 286,112 individuals (52.3%) died. The median survival time for all patients was 49.6 months. Mortality was assessed as a function of presence of a CIED, CIED infection, or form of therapy for CIED infection. Individuals with a CIED were significantly more likely to die of cardiac-related causes than individuals without a CIED (38.0% vs 23.7%, $P < .0001$). Among those with a CIED, individuals with an infected CIED were more likely to die from an infectious cause (11.7% vs 5.7%, $P < .0001$ for infected vs noninfected CIEDs, respectively). Those with an infected CIED who received device extraction within 60 days of the diagnosis were more likely to be alive at the end of the study period as defined above (33.8% vs 26.0%, $P < .0001$, for surgical vs medical therapy, respectively) and less likely to die of an infectious cause (10.0% vs 13.1%, $P < .0001$, for device extraction vs medical therapy, respectively). The median time to death following diagnosis of a CIED infection was 15.7 months versus 9.2 months for those treated via device extraction versus medical therapy, respectively. Device extraction was significantly protective, reducing the hazard of death by 25% (use of HR: 0.75; 95% CI: 0.68–0.82) and controlling for sex, race, ethnicity, atrial fibrillation, CHF, CAD, hepatitis C, bactermia and sepsis, infectious endocarditis, and stroke (Figure 1).

Table 3 Clinical risk factors associated with a cardiac implantable electronic device infection

Risk factor	Adjusted RR	95% CI Lower	95% CI Upper
Race: black vs white	1.08	1.00	1.18
Race: other vs white	0.73	0.60	0.89
Ethnicity: Hispanic vs non-Hispanic	0.76	0.67	0.87
Ethnicity: unknown ethnicity vs non-Hispanic	0.95	0.63	1.44
Age >65 years vs 18–39 years at ESRD diagnosis	0.40	0.34	0.47
Age 40–64 years vs 18–39 years at ESRD diagnosis	0.69	0.58	0.81
Access at first dialysis			
AV graft vs AV fistula	0.93	0.71	1.22
Dialysis catheter vs AV fistula	1.56	1.37	1.78
Other type vs AV fistula	1.61	1.15	2.24
Obesity (BMI >25)	1.13	1.05	1.23

AV = arteriovenous; BMI = body mass index; ESRD = end-stage renal disease; RR = relative risk.

Discussion

In patients undergoing hemodialysis between 2005 and 2009, the rate of infected CIEDs was more than 2 times

Table 4 Likelihood of device extraction versus medical-only therapy of an infected cardiac implantable electronic device

	Adjusted RR*	95% CI Lower	95% CI Upper
Sex: female vs male	0.87	0.80	0.95
Category 1 variables			
Congestive heart failure	1.13	1.01	1.26
Category 3 variables			
Bacteremia	0.89	0.81	0.99
Stroke	0.55	0.38	0.81

*Adjusted relative risks reported.

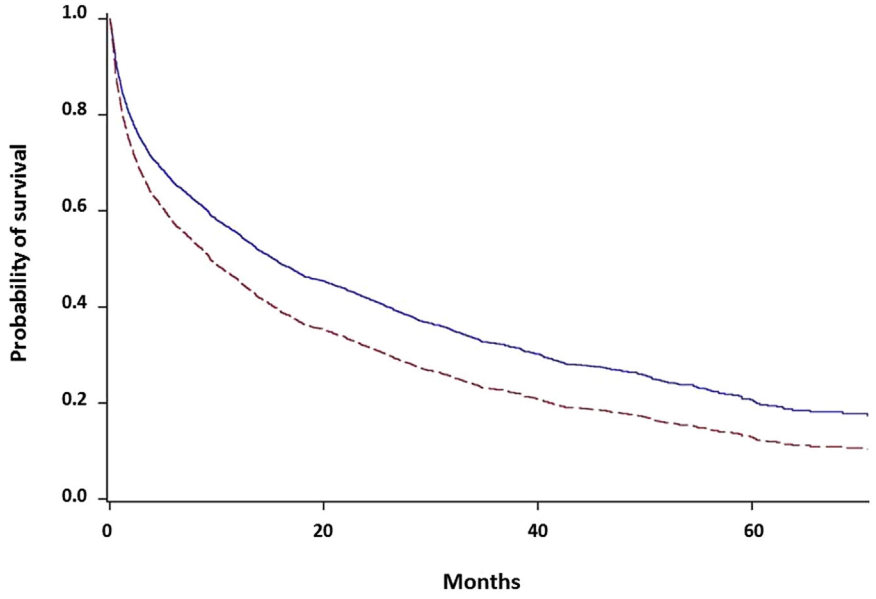

Figure 1 Survival of patients following diagnosis of a cardiac implantable electronic device infection and treated with surgical extraction (solid line) or medical therapy. Surgical extraction conferred a significant survival advantage.

the overall population with CIEDs. Extraction of an infected CIED in dialysis patients resulted in improved survival if accomplished within 60 days of the diagnosis of the infection. The results of this study suggest that device extraction may be underutilized in the ESRD population and support the contention that surgical extraction of an infected CIED confers a survival advantage.

The use of implanted cardiac CIEDs is common in ESRD patients. Approximately 6.4% of more than 540,000 patients in our study population had a CIED. The frequent use of pacemakers or implanted cardioverter-defibrillators in dialysis patients is probably related to the high prevalence of cardiovascular disease and the increased risk of sudden cardiac death in those with ESRD. Sudden cardiac death has been reported at 1.9 deaths per 1000 patient-years in the general population[12] compared to 55 deaths per 1000 patient-years in the ESRD population.[8] All major trials and published guidelines[6] for prevention of sudden cardiac death have excluded patients with ESRD. Therefore we cannot evaluate the appropriateness of the use of CIEDs in our study. However, ESRD patients with CIEDs had cardiovascular conditions similar to the general population with a CIED. As previously reported for the non-ESRD population, a higher percentage of whites received CIEDs compared to African Americans, similar to that observed in the present studies.[13]

ESRD is known to be a risk factor for CIED infection.[5] We would speculate that this may result from frequent bloodstream access for hemodialysis and/or the use of indwelling dialysis catheters.[9] Accordingly, we found that the incidence of CIED infection after initiation of hemodialysis was 8.0%, over 3-fold the national average of 2.4% in 2008.[14] The most frequent group with CIED infection in the USRDS database was younger men. The findings in our study regarding age- and sex-related demographics have been shown in previous studies.[4,15–19] Obesity was also associated with CIED infection. Obesity may contribute to increased risk of CIED infection through several mechanisms, including an increased burden of microbial colonization.[20]

Although complete extraction of the system is usually recommended in patients with CIED infection, those with ESRD have frequent comorbidities that may alter decision making in this setting. Our data show that in ESRD patients with CIED infection, only 26.5% underwent device extraction. Failure to remove the CIED and leads was associated with higher mortality (Figure 1). Medical therapy only for a CIED infection was more common in the presence of bacteremia and stroke. It is not clear from these data why these patients were more frequently treated medically, but we would speculate that these conditions may be surrogate markers for severity of illness, potentially rendering the patients too ill for a procedure. The median time to death following diagnosis of a CIED infection was 15.7 months versus 9.2 months for surgical versus medical treatment. Similar results have been reported previously.[21–25]

Patients with CHF had a higher frequency of device extraction in the event of a CIED infection. This is interesting because the presence of this comorbidity might be expected to increase the risk of device extraction–related complications and potentially mitigate the benefit of system removal. We would speculate that the incidence of implanted cardioverter-defibrillator devices may be higher in CHF patients, and that these cases are thus followed by electrophysiologist cardiologists, who may be more aggressive about extraction. In addition, serious conditions could potentially have swayed the treatment decision toward medical therapy only. These findings go against the theory that the low rate of device extraction was because the patients were too sick to tolerate the procedure. The issue of whether

comorbidities increase the relative risk of device extraction or increase the relative benefit in those at highest risk is a subject of ongoing debate.[26,27]

The mortality differences between medical treatment alone and device extraction declined over time, the longer a patient survived following the initial diagnosis of device infection. Notably, overall mortality was reduced by 25% in patients undergoing device extraction within the first 60 days after CIED infection was identified when compared to medical therapy. We show that, over time, ESRD patients have a poor mortality regardless of disease management; however, in the short term, extraction offers a better outcome over medical therapy.

Limitations

This is a retrospective cohort analysis that does not allow us to directly compare the efficacy of medical and surgical treatment strategies. The reasons for choosing one strategy over the other cannot be ascertained from an administrative database. All diagnoses and procedures were inferred from billing codes and are not the result of actual medical documentation. In this regard, code 996.61 may be subject to some ambiguities in diagnoses. Despite its clear designation as a billing code for "infection and inflammatory reaction due to cardiac device, implant, and graft," there may be other infected or inflamed states that may potentially be classified under this code (for example, stitch abscess or wound cellulitis) and thus allow patients with minor infectious complications to contaminate the group with CIED infection. These patients would be expected to expand the total population of infected patients, but would likely increase the number treated medically (ie, without device extraction), and thus reflect successes in the medical approach. Their presence in the total pool of infected patients would not be expected to alter the results or conclusion that surgical extraction is associated with improved survival. Likewise, patients with an infected lead but without a pocket infection may have been coded as bacteremic or septic. We do not know the incidence of this coding issue; however, if the lead was not removed, the patients would have been relegated to the medical therapy group, which demonstrated a poorer prognosis than those patients with a lead extraction. In general, a major limitation of drawing scientific conclusions from administrative datasets is the uncertainty in coding accuracies. This constraint is balanced against the advantages of a large dataset such as the USRDS, including the population-based nature of the data, a fairly complete dataset, and the relative availability of the data.[28,29]

Conclusion

Many ESRD patients have CIEDs, and infections of these devices are twice as frequent as in patients not on dialysis. Outcomes of CIED infection in this population are poor, with average survival <1 year. Device extraction within 60 days of diagnosed CIED infection is associated with a modest improvement in survival. However, the condition has a high mortality regardless of device extraction.

Appendix

Supporting data

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.hrthm.2015.08.003.

References

1. Masoudi FA, Ponirakis A, Yeh RW, et al. Cardiovascular care facts: a report from the national cardiovascular data registry: 2011. J Am Coll Cardiol 2013;62:1931–1947.
2. Greenspon AJ, Patel JD, Lau E, Ochoa JA, Frisch DR, Ho RT, Pavri BB, Kurtz SM. Trends in permanent pacemaker implantation in the United States from 1993 to 2009: increasing complexity of patients and procedures. J Am Coll Cardiol 2012;60:1540–1545.
3. Tonelli M, Wiebe N, Culleton B, House A, Rabbat C, Fok M, McAlister F, Garg AX. Chronic kidney disease and mortality risk: a systematic review. J Am Soc Nephrol 2006;17:2034–2047.
4. Uslan DZ, Sohail MR St, Sauver JL, Friedman PA, Hayes DL, Stoner SM, Wilson WR, Steckelberg JM, Baddour LM. Permanent pacemaker and implantable cardioverter defibrillator infection: a population-based study. Arch Intern Med 2007;167:669–675.
5. Athan E, Chu VH, Tattevin P, et al. Clinical characteristics and outcome of infective endocarditis involving implantable cardiac devices. JAMA 2012;307:1727–1735.
6. Epstein AE, DiMarco JP, Ellenbogen KA, et al. American College of Cardiology/American Heart Association Task Force on Practice G, American Association for Thoracic S and Society of Thoracic S. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices): developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. Circulation 2008;117:e350–e408.
7. Baddour LM, Epstein AE, Erickson CC, et al. American Heart Association Rheumatic Fever E, Kawasaki Disease C, Council on Cardiovascular Disease in Y, Council on Cardiovascular S, Anesthesia, Council on Cardiovascular N, Council on Clinical C, Interdisciplinary Council on Quality of C and American Heart A. Update on cardiovascular implantable electronic device infections and their management: a scientific statement from the American Heart Association. Circulation 2010;121:458–477.
8. In: Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2010. USRDS 2010 Annual Data Report.
9. Tokars JI, Light P, Anderson J, Miller ER, Parrish J, Armistead N, Jarvis WR, Gehr T. A prospective study of vascular access infections at seven outpatient hemodialysis centers. Am J Kidney Dis 2001;37:1232–1240.
10. Girndt M, Sester U, Sester M, Kaul H, Kohler H. Impaired cellular immune function in patients with end-stage renal failure. Nephrol Dial Transplant 1999;14:2807–2810.
11. Zou G. A modified Poisson regression approach to prospective studies with binary data. Am J Epidemiol 2004;159:702–706.
12. Rea TD, Pearce RM, Raghunathan TE, Lemaitre RN, Sotoodehnia N, Jouven X, Siscovick DS. Incidence of out-of-hospital cardiac arrest. Am J Cardiol 2004;93:1455–1460.
13. Cabell CH, Heidenreich PA, Chu VH, Moore CM, Stryjewski ME, Corey GR, Fowler VG Jr. Increasing rates of cardiac device infections among Medicare beneficiaries: 1990-1999. Am Heart J 2004;147:582–586.
14. Greenspon AJ, Patel JD, Lau E, Ochoa JA, Frisch DR, Ho RT, Pavri BB, Kurtz SM. 16-year trends in the infection burden for pacemakers and implantable cardioverter-defibrillators in the United States 1993 to 2008. J Am Coll Cardiol 2011;58:1001–1006.
15. Lai KK, Fontecchio SA. Infections associated with implantable cardioverter defibrillators placed transvenously and via thoracotomies: epidemiology, infection control, and management. Clin Infect Dis 1998;27:265–269.
16. Catanchin A, Murdock CJ, Athan E. Pacemaker infections: a 10-year experience. Heart Lung Circ 2007;16:434–439.
17. Lekkerkerker JC, van Nieuwkoop C, Trines SA, van der Bom JG, Bernards A, van de Velde ET, Bootsma M, Zeppenfeld K, Jukema JW, Borleffs JW, Schalij MJ, van Erven L. Risk factors and time delay associated with cardiac device infections: Leiden device registry. Heart 2009;95:715–720.

18. Klug D, Balde M, Pavin D, et al. Risk factors related to infections of implanted pacemakers and cardioverter-defibrillators: results of a large prospective study. Circulation 2007;116:1349–1355.
19. Nori US, Manoharan A, Thornby JI, Yee J, Parasuraman R, Ramanathan V. Mortality risk factors in chronic haemodialysis patients with infective endocarditis. Nephrol Dial Transplant 2006;21:2184–2190.
20. Akinnusi ME, Pineda LA, El Solh AA. Effect of obesity on intensive care morbidity and mortality: a meta-analysis. Crit Care Med 2008;36:151–158.
21. Charytan DM, Patrick AR, Liu J, Setoguchi S, Herzog CA, Brookhart MA, Winkelmayer WC. Trends in the use and outcomes of implantable cardioverter-defibrillators in patients undergoing dialysis in the United States. Am J Kidney Dis 2011;58:409–417.
22. Baddour LM. Infectious Diseases Society of America's Emerging Infections N. Long-term suppressive antimicrobial therapy for intravascular device-related infections. Am J Med Sci 2001;322:209–212.
23. Lin JC, Aung G, Thomas A, Jahng M, Johns S, Fierer J. The use of ceftaroline fosamil in methicillin-resistant Staphylococcus aureus endocarditis and deep-seated MRSA infections: a retrospective case series of 10 patients. J Infect Chemother 2013;19:42–49.
24. Lopez JA. Conservative management of infected pacemaker and implantable defibrillator sites with a closed antimicrobial irrigation system. Europace 2013;15:541–545.
25. Puri R, Psaltis PJ, Nelson AJ, Sanders P, Young GD. Povidone-iodine irrigation - a possible alternative to lead extraction. Indian Pacing Electrophysiol J 2011;11:115–119.
26. Rodriguez Y, Garisto J, Carrillo RG. Management of cardiac device-related infections: a review of protocol-driven care. Int J Cardiol 2013;166:55–60.
27. Brunner MP, Cronin EM, Duarte VE, et al. Clinical predictors of adverse patient outcomes in an experience of more than 5000 chronic endovascular pacemaker and defibrillator lead extractions. Heart Rhythm 2014;11:799–805.
28. Hertzer NR. Reasons why data from the Nationwide Inpatient Sample can be misleading for carotid endarterectomy and carotid stenting. Semin Vasc Surg 2012;25(1):13–17.
29. Potter BK, Manuel D, Speechley KN, Gutmanis IA, Campbell MK, Koval JJ. Is there value in using physician billing claims along with other administrative health care data to document the burden of adolescent injury? An exploratory investigation with comparison to self-reports in Ontario, Canada. BMC. Health Serv Res 2005;5(1):15.

CLINICAL PERSPECTIVES

To our knowledge, this is the largest study to date of end-stage renal disease (ESRD) patients and the associated risk factors for cardiac implantable electronic device (CIED) infections. This study reveals that CIED infection in ESRD patients is common and that management strategies vary widely, with device and lead extraction being underutilized. Given the improvement in mortality that extraction seems to afford in this study, early referral for consideration of extraction in this population is important. Further study into barriers for referral for extraction is needed and will help in understanding how to better manage this underserved population.