Permanent Pacemaker and Implantable Cardioverter Defibrillator Infection

A Population-Based Study

Daniel Z. Uslan, MD; Muhammad R. Sohail, MD; Jennifer L. St. Sauver, PhD; Paul A. Friedman, MD;
David L. Hayes, MD; Sarah M. Stoner, MS; Walter R. Wilson, MD; James M. Steckelberg, MD; Larry M. Baddour, MD

Background: The incidence of cardiac device infection is not well understood. Bloodstream infection (BSI) in patients with permanent pacemakers or implantable cardioverter-defibrillators (hereafter, defibrillators) may reflect device infection.

Methods: Retrospective, population-based cohort study of all adult patients with cardiac devices who resided in Olmsted County, Minnesota, from 1975 to 2004. The medical linkage-system of the Rochester Epidemiology Project and standardized criteria were used to identify all cases of BSI and device infection. The incidence of device infection was calculated with person-years of follow-up after device implantation.

Results: A total of 1524 patients with cardiac devices were included in the cohort. Total person-time of follow-up was 7578 years. The incidence of definite device infection was 1.9 per 1000 device-years (95% confidence interval [CI], 1.1-3.1). The incidence of pocket infection without BSI was 1.37 per 1000 device-years (95% CI, 0.62-3.05), and pocket infection with BSI or device-related endocarditis 1.14 per 1000 device years (95% CI, 0.47-2.74). The cumulative probability of device infection was higher among patients with defibrillators compared with those with pacemakers, *P*<.001. Twelve (54.6%) of 22 cases of *Staphylococcus aureus* BSI had definite or possible cardiac device infection vs 3 (12.0%) of 25 cases of bloodstream infection due to gram-negative bacilli (*P*=.004).

Conclusions: To our knowledge, this is the first population-based study to describe the incidence of cardiac device infection. Device infection was common during episodes of *S aureus* BSI. The rate of cardiac device infection was higher in patients with defibrillators than in those with pacemakers.

Arch Intern Med. 2007;167:669-675

Author Affiliations:
Department of Medicine, Divisions of Infectious Diseases (Drs Uslan, Wilson, Steckelberg, and Baddour) and Cardiovascular Diseases (Drs Friedman and Hayes), and Department of Health Sciences Research (Dr St. Sauver and Ms Stoner), Mayo Clinic College of Medicine, Rochester, Minn; and Division of Infectious Diseases, Department of Medicine, Tawam Hospital/Johns Hopkins Medicine, Al Ain, United Arab Emirates (Dr Sohail). Dr Uslan is now with the Division of Infectious Diseases, University of California, Los Angeles, David Geffen School of Medicine at UCLA.

THE ESTIMATED RATE OF CARdiac device infection after permanent endocardial pacemaker (PPM) or implantable cardioverter-defibrillator (hereafter, defibrillator) implantation has varied from 0.13% to 19.9%[1,2] but has increased by 124% over the past decade.[3] Prior studies, however, have been limited by lack of person-time data, and these rates are difficult to interpret. Results from treatment with prolonged parenteral antibiotics in the absence of hardware removal have thus far been disappointing.[4-9] Therefore, the prevailing opinion is to remove the complete device system if infection is confirmed.[10,11] Accurate diagnosis of device infection is essential to ensure that patients with infection are treated appropriately, including device removal if indicated. A correct diagnosis is equally important among patients who do not have device infection so that unnecessary device removal does not occur because many patients are device dependent, and life-threatening complications of device removal can occur.[4,12,13]

Alternative sources of bloodstream infection (BSI) other than that caused by primary device infection can result in secondary infection of the intravascular portion of the lead. These sources include contaminated vascular catheters and other types of infected indwelling cardiovascular devices and infections at other sites, including the urinary, hepatobiliary, gastrointestinal, and respiratory tracts. Neither the incidence of BSI nor its impact on the therapeutic approach to treatment of device infection have been adequately evaluated.

We conducted a large retrospective population-based cohort study to define the incidence and clinical manifestations of device infection in patients with car-

diac devices and BSI in Olmsted County, Minnesota. Our aim was to address 2 major unanswered questions in the study of device infection: *What is the incidence rate of device infection in patients with BSI, and does this rate differ based on organism or device type?*

METHODS

SETTING

The Rochester Epidemiology Project (REP) is a medical record-linkage system that indexes medical records from all individuals residing in Olmsted County. A single dossier exists for each patient and into it medical diagnoses, surgical interventions, and other key information from medical records are regularly abstracted and entered into computerized indices using the *International Classification of Diseases, Adapted Code for Hospitals*.[14,15] Because the REP provides access to details of health care of local residents regardless of health provider, accurate incidence data and population-based analytic studies of disease causes and outcomes are possible.[15] Included in REP dossiers are medical histories and diagnoses for all patient encounters within the health care system, including both hospitals (Mayo Clinic and Olmsted Medical Center, Rochester).

CASE ASCERTAINMENT

The Division of Cardiovascular Diseases at Mayo Clinic maintains prospectively collected databases of cardiac device implantations as well as follow-up patient encounters. Because Mayo Clinic is the only institution in Olmsted County that performs cardiac implantation or follows up patients with cardiac devices, virtually all residents of Olmsted County with cardiac devices would have undergone implantation at Mayo Clinic. Patients with cardiac devices implanted elsewhere who then relocated to Olmsted County would be included if they had ever received medical care related to their device. No patients with cardiac resynchronization devices were included in the study.

Cases of BSI were identified using several methods. Electronic blood culture data were available from both microbiology laboratories in Olmsted County (for Mayo Clinic from 1983 to the present and Olmsted Medical Center from 2003 to the present) and were matched to cardiac device databases. For study years without electronic data available, we used adapted *International Classification of Diseases, Ninth Revision (ICD-9)* codes[16] for conditions such as bacterial infections, urinary tract infection, pneumonia, sepsis, and bacteremia to identify patients who may have potentially had BSI. These medical records were then manually reviewed to ascertain the presence of BSI. A wide range of diagnostic codes was used to ensure that all potential cases of BSI would be captured, minimizing missed cases. Once cases of BSI were identified via either of these methods, medical records were then manually reviewed to assess possible device infection. Any cases of BSI or device infection judged to be problematic were reviewed with an experienced investigator (L.M.B.).

CASE DEFINITIONS

Identification of device infection may be challenging for physicians given the wide variety of presenting syndromes and lack of a diagnostic gold standard. We used the definition by Chamis et al[9] previously well described in other studies of device infection.[17] Clinical evidence of device infection included local signs of inflammation at the generator pocket, including erythema, warmth, fluctuance, wound dehiscence, tenderness, purulent drainage, or erosion of the generator or lead through the skin. Endocarditis was diagnosed if valvular or lead vegetations were detected by echocardiography or if the modified Duke criteria for infective endocarditis were met.[18,19] Device infection was microbiologically confirmed if findings from culture samples or gram stain from the generator pocket or electrode lead were positive for organisms. Device infection was rejected if the patient had no evidence of device infection at the time of the initial BSI, the device was not removed, and there was no evidence of BSI relapse within 12 weeks. For patients who died during hospitalization, a diagnosis of device infection was rejected if no evidence of device infection was detected at autopsy. Device infection was defined as "possible" if death occurred prior to confirmation or rejection.

Given that contaminated blood cultures may represent up to half of all blood cultures with microbial growth,[20-23] we applied a definition of contamination previously described by Bekeris et al.[24] A blood culture was considered to be contaminated if 1 or more of the following were identified in only 1 bottle of a series of blood culture specimens: coagulase-negative *Staphylococcus* species, *Propionibacterium acnes*, *Micrococcus* species, viridans-group streptococci, *Corynebacterium* species, or *Bacillus* species. A blood culture series was defined as 1 or more specimens collected serially within a 24-hour period to detect an episode of BSI. Patients with contaminated blood culture specimens were not included as incident cases. Bloodstream infections were classified as nosocomial, health care–associated, or community-acquired using definitions previously described.[25] Nosocomial BSI was defined as BSI in patients who had been hospitalized for 48 hours or longer. Health-care associated BSI was defined as BSI in patients receiving home intravenous therapy, dialysis, or intravenous chemotherapy, or residing in a nursing home or long-term care facility. Community-acquired BSI was diagnosed on admission to the hospital, or within the first 48 hours, in patients not meeting the definition of health care–associated BSI.

VALIDITY AND RELIABILITY OF METHODS

We conducted several small-scale validity studies of our case-finding procedure. First, we tested whether our indexing system was sensitive, that is, whether diagnoses of BSI obtained via adapted *ICD-9* codes[16] missed cases of true BSI as obtained from microbiology records. We compared all Olmsted County residents (regardless of cardiac device status) identified as potential BSI cases via adapted *ICD-9*[16] codes from 2003 to 2004 with computerized blood culture data from both microbiology laboratories over the same time period. Of 103 patients identified via the microbiology laboratories, 102 cases (99%) were captured with adapted *ICD-9* codes.[16]

Second, to assess the reliability of ascertainment of device infection, the cases of 20 patients with cardiac devices and BSI selected at random were independently reviewed by a senior investigator (L.M.B.) who was unaware of the classification made by the primary investigator (D.Z.U.). There was 100% inter-abstractor agreement, indicating that our definition of device infection was highly reproducible.

DATA ANALYSIS

Incidence rates of BSI were calculated using incident cases of BSI as the numerator and person-years of device implantation as the denominator, as determined via the methods described in the "Case Definitions" subsection. Patients were counted twice only if the second BSI was due to a different organism; patients with 2 separate BSIs due to the same organism were considered to have relapsed. Device implantation rates were derived using the population from decennial census figures as the

Table 1. Demographic Characteristics of 1503 Patients With Permanent Pacemaker (PPM) or Defibrillator, 1975-2004*

	Patients	
Characteristic	**1300 With PPM**	**203 With Defibrillator**
Male sex, No. (%)	632 (49)	165 (81)
Age at device implant, mean (SD), y	76.2 (12.5)	64.3 (14.4)
Charlson Comorbidity Index, median (interquartile range)†	3 (2-6)	NA
Survival after device placement, median, y	6.28	8.93
Bloodstream infection, No. (%)	63 (4.8)	12 (5.9)

Abbreviation: NA, not available.
*Excluding patients with both PPM and defibrillator.
†The Charlson Comorbidity Index was calculated from administrative databases, as previously described.[26] Data for the Charlson Comorbidity Index were available for only 1146 of the patients with PPM.

Figure 1. Incidence of cardiac device implantation, Olmsted County, Minnesota, 1975-2004 (age adjusted to the population of white individuals in the United States in 2000).

denominator, with a population growth rate of 1.9% projected for years after 2000. Person-years at risk were calculated from the date of device implantation to the date of BSI, death, or censoring (for example, if the patient left Olmsted County). The association between BSI, device infection, and survival was examined by Kaplan-Meier survival curves and multivariate Cox regression analysis, adjusting for age, sex, and device type. Fisher exact tests were used for comparison between proportions. The level of significance for all statistical tests was 2-sided, at $P<.05$. The institutional review boards of both Mayo Clinic and Olmsted Medical Center approved the study.

RESULTS

A total of 1524 patients with cardiac devices were identified in Olmsted County during the study period and were included in the cohort. Patient characteristics are described in **Table 1**; 1300 patients had PPMs, 203 had defibrillators, and 21 patients had both. The mean (SD) age at device placement was 74.6 (13.5) years overall, although there was a significant difference between mean age of patients with PPMs (76.2 years; 95% confidence interval [CI], 75.5-76.9) and those with defibrillators (64.3 years; 95% CI, 62.4-65.9) ($P<.001$). Of the PPM recipients, 51% were female, whereas only 19% of defibrillator recipients were female ($P<.001$).

Incidence of device implantation in Olmsted County (age-adjusted to the population of white individuals in the United States in 2000) over the 30-year period is shown in **Figure 1**. Total person-time of follow-up from device placement to infection, death, or censoring was 7578.4 years. The median duration of survival after device placement via Kaplan-Meier analysis was 6.93 years. The median duration of survival by type of device implanted first was 8.93 years for defibrillator and 6.40 years for PPM; however, after adjusting for age at implantation and sex via Cox proportional hazards regression, there was no statistically significant difference in survival for patients with defibrillator vs PPM (data not shown).

To assess the incidence of pocket infection without BSI, we looked at a subset of the full cohort. Because patients with pocket infection often may not have BSI and
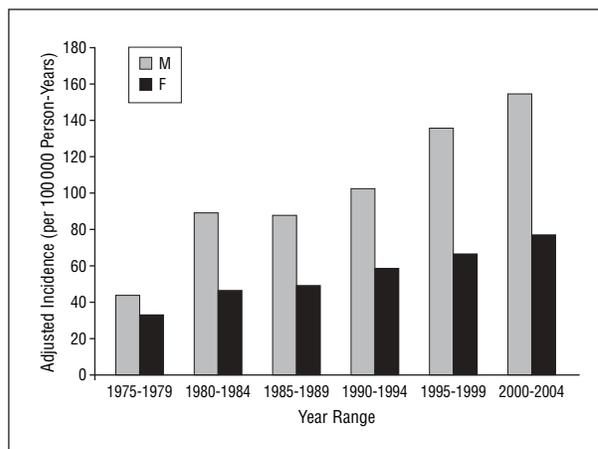
Table 2. Microbiologic Distribution of 78 Bloodstream Infections in 75 Patients With Cardiac Devices

Organism	Infections, No. (%)
Staphylococcus aureus	22 (28)
Escherichia coli	17 (22)
Klebsiella species	7 (9)
Enterococcus species	6 (8)
β-Hemolytic streptococci	6 (8)
Coagulase-negative staphylococci	5 (6)
Streptococcus pneumoniae	4 (5)
Citrobacter species	3 (4)
Other*	8 (10)

*Includes viridans-group streptococci, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Listeria monocytogenes*, *Bacteroides* species, and *Clostridium* species.

would therefore not be identified by our methods, we manually reviewed the records of device patients from 1991 (the first year electronic records were available) through 2005 as previously described.[27] Of the 1524 patients from the full cohort, 1087 were included, of whom 879 had PPM, 203 had defibrillators, and 5 had both. There were 6 pocket infections without BSI identified in 4376.7 total device-years of follow-up from time of implantation to time of pocket infection or censoring (incidence rate, 1.37 per 1000 device-years; 95% CI, 0.62-3.05).

Of the 1524 patients in the full 30-year cohort, 78 cases of BSI occurred in 75 unique patients. The incidence of BSI was 10.1 per 1000 device-years (95% CI, 8.1-12.7). Specific organisms are given in **Table 2**. The most common organisms were *Staphylococcus aureus* (22 cases of BSI [28%]) and *Escherichia coli* (17 cases of BSI [22%]). In 9 cases (40%), *S aureus* isolates were methicillin resistant. Bloodstream infection occurred a median of 1140 days (range, 22-7110 days) after device implantation. The cumulative probability of BSI after device implantation is shown in **Figure 2**. Suspected sources included the urinary tract (22 cases of BSI [28%]), central venous catheters (12 cases [15%]),
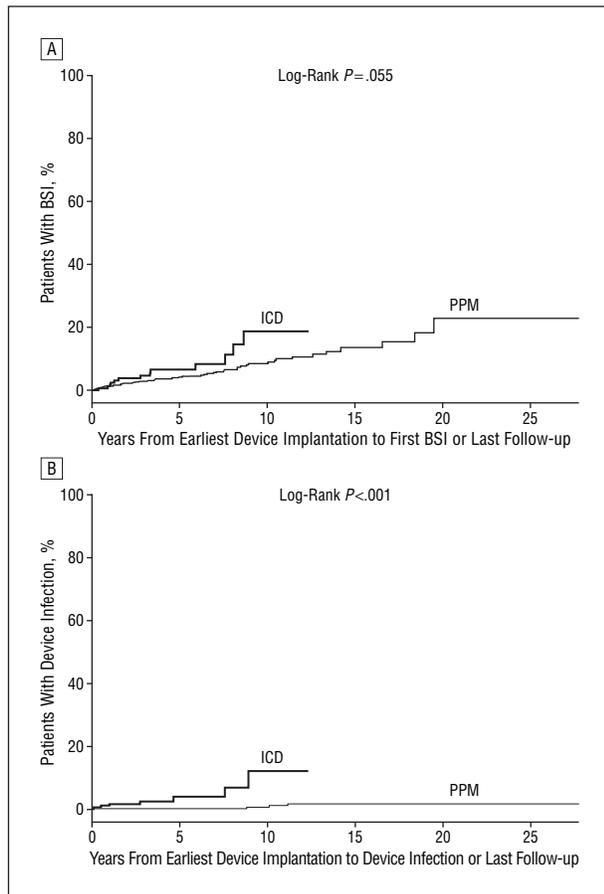
Figure 2. Cumulative probability of bloodstream infection (BSI) (using Kaplan-Meier method) in patients with an implantable cardioverter-defibrillator (ICD) vs those with a permanent pacemaker (PPM). A, Cumulative probability of BSI; B, definite device infection.

Table 3. Clinical Characteristics of 75 Patients With Bloodstream Infection (BSI)*

| | Patients | | |
	With Defibrillator (n = 13)	With PPM (n = 62)	P Value
Demographics			
Male sex	12 (92.3)	37 (59.7)	.03
Age at device implantation, mean (SD), y	66.4 (11.1)	76.4 (9.2)	.004
Device characteristics			
Generator site			
Left chest	12 (92.3)	54 (87.1)	
Right chest	1 (7.7)	6 (9.7)	>.99
Abdomen	0	2 (3.3)	
>1 Lead at time of BSI	8 (61.5)	34 (54.8)	>.99
Complication during placement†	1 (7.7)	2 (3.3)	.45
>1 Total device-related procedures‡	5 (38.5)	15 (24.2)	.32
Host factors			
Diabetes mellitus	5 (38.5)	13 (20.9)	.28
Hemodialysis	2 (15.4)	8 (12.9)	.64
Central venous catheter	4 (30.7)	10 (16.2)	.25
Malignancy	5 (38.5)	17 (27.4)	.51
Coronary artery disease	12 (92.3)	36 (58.5)	.02
Coronary artery bypass graft	6 (46.2)	9 (14.5)	.02
Congestive heart failure	9 (69.3)	35 (56.5)	.54
Prosthetic heart valve	2 (15.4)	8 (12.9)	.64
Atrial fibrillation	3 (27.3)	29 (45.3)	.34
Anticoagulation§	2 (15.4)	20 (32.3)	.32
Chronic obstructive pulmonary disease	5 (38.5)	15 (24.2)	.32
Intravenous drug abuse	0	0	>.99
History of device infection	0	1 (1.6)	>.99
BSI characteristics			
Nosocomial	2 (15.4)	5 (8.0)	
Health care–associated	6 (46.1)	43 (69.4)	.29
Community-acquired	5 (38.5)	14 (22.6)	

Abbreviation: PPM, permanent pacemaker.
*Data are presented as number (percentage) except where noted.
†Complication defined as excessive bleeding, hemodynamic instability requiring intervention, arrhythmia requiring defibrillation, or resuscitation.
‡Includes battery or generator changes, lead replacement, or revision.
§Excluding aspirin.

pneumonia (8 cases [10%]), intra-abdominal (7 cases [9%]), skin or soft-tissue (6 cases [8%]), or other or unknown source (23 cases [30%]). Risk factors and clinical characteristics of the 75 patients with BSI are described in **Table 3**.

Echocardiography was performed in 33 episodes of BSI (42%), including transthoracic echocardiography in 10 episodes, transesophageal echocardiography in 17 episodes, and both transthoracic and transesophageal in 6 episodes. Six (18%) of the 33 patients who had echocardiograms had vegetations noted on echocardiography, including 2 cases with lead vegetations, 2 with valvular vegetations, and 2 with vegetations on both lead and valve. All patients with vegetations had undergone transesophageal echocardiography; valvular vegetations were seen on the tricuspid valve (2 cases), mitral valve (1 case), and the aortic valve (1 case). None of the 10 patients who had only transthoracic echocardiography had vegetations demonstrated. Six patients (18%) met modified Duke criteria for infective endocarditis.[18,19]

Seven definite device infections were diagnosed by clinical or microbiologic criteria in patients with BSI. Comparison of clinical features of BSI cases with and without definite device infection is shown in **Table 4**. Causative organisms included coagulase-negative staphylococci (2 cases), *S aureus* (4 cases), and enterococci (1 case).

None of the episodes of BSI due to gram-negative bacilli were associated with definite device infection. Two patients with gram-negative BSI developed relapsing bacteremia after cessation of antimicrobial therapy; alternative explanations for relapse other than device infection were noted in both (biliary obstruction due to malignancy in 1 patient and chronic indwelling urinary catheter in the other). Neither of the patients underwent echocardiographic evaluation during their initial BSI.

Of the 22 patients with *S aureus* BSI, 4 (18%) met criteria for definite device infection vs none of the patients with gram-negative bacilli BSI (*P*=.04). Two (3%) of 62 patients with PPMs with BSI had device infection vs 5 (36%) of 14 patients with defibrillators (*P*=.002). Median duration of follow-up after BSI was 252 days (range, 0-4594 days; intraquartile range, 52-1030). Fifty-one (72%) of the patients had a duration of follow-up greater than 12 weeks without evidence of recurrent infection, and a diagnosis of device infection was therefore re-

jected. Of the remaining 20 patients with duration of follow-up of less than 12 weeks, 15 (75%) died while in the hospital. Three had autopsies that showed no evidence of device infection. Two patients (1 with *Streptococcus agalactiae* BSI and 1 with *S aureus* BSI) had evidence of mitral valve infective endocarditis at autopsy but showed no specific histopathologic evidence of cardiac device infection. These 2 patients were classified as having possible device infection; the other 3 with autopsies that were negative for infection were classified as not having device infection.

Comparison of rates of device infection among *S aureus*, gram-negative bacilli, and other organisms is shown in **Table 5**. The rate of possible or definite device infection in patients with *S aureus* BSI was 12 (55%) of 22; in patients with BSI owing to gram-negative bacilli, it was 3 (12%) of 25 (*P*=.004).

Overall, the incidence rate of pocket infection alone was 1.37 per 1000 device-years; the incidence rate of device-related endocarditis or pocket infection with BSI was 1.14 per 1000 device-years. The cumulative probability of device infection is shown in Figure 2. The cumulative probability of device infection was higher among those with a defibrillator compared with those with a PPM (*P*<.001). The incidence of definite device infection was 1.9 per 1000 device-years (95% CI, 1.1-3.1). The incidence of defibrillator infection was 8.9 (95% CI, 4.2-18.6) per 1000 device-years; the incidence of PPM infection was 1.0 (95% CI, 0.5-2.2) per 1000 device-years (*P*<.001).

COMMENT

The present study is the largest to date of infection in patients with cardiac devices and to our knowledge is the first to calculate the incidence of device infection in a population-based setting. This design eliminates the tertiary referral bias typically seen in other studies of device infection. In our large cohort study spanning a 30-year time period of over 7500 device-years of follow-up, the incidence of device infection was 1.9 per 1000 device-years.

To our knowledge, our study is the first to directly compare the incidence of device infection in patients with BSI caused by varying pathogens. The estimated rate of device infection in patients with *S aureus* BSI was estimated at as much as 54.6%, similar to previously reported investigations.[5,9] The low risk of device infection among patients with BSI caused by gram-negative bacilli is similar to our previously published non–population-based investigation.[28] These findings have profound implications for physicians who care for patients with cardiac devices. It is unclear if differential rates of infection during BSI caused by varying pathogens are due to intrinsic pathogen-related factors (such as adherence factors and biofilm formation),[11,29,30] device-specific characteristics, or host factors such as time to BSI after implantation, age, or sex. Previous studies of bacterial adherence to heart valves in vivo found similar differences between gram-positive and gram-negative organisms.[31] An alternative explanation is that device infection does occur with BSI due to gram-negative bacilli, but antimicrobial therapy

Table 4. Comparison of Demographic and Clinical Features of Device Infection Among 78 Cases of Bloodstream Infection (BSI)*

	Cases of BSI		
Risk Factor	Definite Device Infection (n = 7)	No Device Infection (n = 71)	*P* Value
Male sex	5 (71.4)	46 (65.8)	>.99
Age, mean (SD), y	70.8 (16.6)	79.4 (9.9)	.24
Implantable cardioverter defibrillator	5 (71.4)	9 (12.7)	.002
>1 Lead	2 (28.6)	42 (59.2)	.23
Diabetes mellitus	3 (42.8)	16 (22.5)	.35
Hemodialysis	4 (57.1)	7 (9.8)	.006
Central venous catheter	4 (57.1)	11 (15.5)	.02
Malignancy	1 (14.3)	22 (31.0)	.67
Coronary artery disease	7 (100)	43 (60.6)	.045
Prosthetic valve	3 (42.9)	9 (12.7)	.07
Atrial fibrillation	3 (42.9)	29 (40.9)	>.99
Anticoagulation	0	23 (32.4)	.09
Congestive heart failure	5 (71.4)	40 (56.3)	.73
WBC (×10³/mL), median (95% CI)	11 100 (6700-15 500)	14 500 (12 600-16 400)	.17

Abbreviations: CI, confidence interval; WBC, white blood cell count.
*Data are presented as number (percentage) except where noted.

Table 5. Comparison of Device Infection Cases Among 78 Cases of Bloodstream Infection (BSI)

	Cases of BSI, No. (%)		
Device Infection*	*Staphylococcus aureus* (n = 22)	Gram-Negative Bacilli (n = 25)	Other Organisms† (n = 31)
Definite	4 (18)	0	4 (10)
Possible	8 (36)	3 (12)	1 (3)
Rejected	10 (45)	22 (88)	26 (84)

P value for difference in rate of device infection between *S aureus* and gram-negative BSI is .004.
†Definite or possible cases included coagulase-negative staphylococci (2 cases), *Enterococcus*, *Streptotoccus agalactiae*, and *Fusobacterium nucleatum*.

is curative, even if the system is infected and not removed. Understanding the difference in rates of device infection during BSI caused by different organisms may help avoid unnecessary device removal in patients who are device dependent, which is especially important because morbidity and mortality with device removal are well described.[4,12,13]

Surprisingly, we found that the cumulative probability of device infection was significantly higher in patients with defibrillators compared with those with PPMs. It is unclear if this is due to underlying comorbidities or demographics of patients with defibrillators, differences in device or lead physical properties, or implantation-associated risks (such as increased procedure complexity, length of procedure, or physician volume[32]). Recent data on device exchanges related to manufacturer recalls suggest a higher rate of infection in these

patients.[33] Further understanding of the specific risk factors for device infection will be crucial.

The present study has several limitations that are primarily the result of its retrospective design. Olmsted County has relatively homogeneous demographics, which may limit the generalizability to populations underrepresented in the community.[15] Usage of adapted *ICD-9* codes[16] for screening of potential cases of BSI has not been previously validated, although the internal validity of our methods seemed to be excellent when compared with computerized microbiology data. Computerized microbiology records were used for Mayo Clinic patients from 1983 to 2005, and therefore *ICD-9* codes[16] represented a very small portion of our cases. Transesophageal echocardiography was not performed in all patients (or even available for clinical practice during the early years of our study) and may have been differentially undertaken in patients who were considered to be at higher risk for device infection. We attempted to address this limitation by using criteria, including follow-up without relapse and autopsy findings in deceased patients, to improve case ascertainment. Although the lack of universal echocardiography precludes an exact calculation of the rate of device infection owing to varying pathogens, the long duration of follow-up that is available with a population-based study effectively excluded device infection in most of our patients. Even if device infection were present in all patients who did not undergo echocardiography, it would not have a clinical impact on the treatment of these patients because relapses were uncommon.

Microbiologic techniques, such as the volume of blood collected, number of bottles, duration of incubation, and methods of bacterial identification, have changed over time. It is difficult to assess what impact, if any, this would have had on our study. Only patients whose blood cultures were positive for organisms were included. Patients who may have clinically been considered to have sepsis but whose blood cultures were negative for organisms were therefore not included, nor were those whose cultures were negative for organisms owing to preceding therapy with antimicrobial drugs. Patients with BSI who did not have blood cultures drawn (eg, those who did not seek medical attention or were treated empirically without culture samples) or patients with transient BSI, such as BSI following a medical procedure, would have been missed as well. Our results then would be an underestimation of the true incidence of BSI in this population.

Prior studies have supported the systematic extraction of cardiac devices among patients with device infection, followed by prolonged therapy with antimicrobial drugs prior to device reimplantation at a new site.[5,9,10] Our data support the consideration of device infection among patients with *S aureus* BSI, but device infection, or the necessity for device removal, does not seem to be commonly found in patients with BSI caused by gram-negative bacilli.

Correspondence: Daniel Z. Uslan, MD, Division of Infectious Diseases, David Geffen School of Medicine at UCLA, 10833 LeConte Ave, 37-121 CHS, Los Angeles, CA 90095 (duslan@mednet.ucla.edu).

REFERENCES

1. Conklin EF, Giannelli S Jr, Nealon TF Jr. Four hundred consecutive patients with permanent transvenous pacemakers. *J Thorac Cardiovasc Surg.* 1975;69:1-7.
2. Bluhm G. Pacemaker infections: a clinical study with special reference to prophylactic use of some isoxazolyl penicillins. *Acta Med Scand Suppl.* 1985;699:1-62.
3. Cabell CH, Heidenreich PA, Chu VH, et al. Increasing rates of cardiac device infections among Medicare beneficiaries: 1990-1999. *Am Heart J.* 2004;147:582-586.
4. Arber N, Pras E, Copperman Y, et al. Pacemaker endocarditis: report of 44 cases and review of the literature. *Medicine.* 1994;73:299-305.
5. Camus C, Leport C, Raffi F, Michelet C, Cartier F, Vilde JL. Sustained bacteremia in 26 patients with a permanent endocardial pacemaker: assessment of wire removal. *Clin Infect Dis.* 1993;17:46-55.
6. Cacoub P, Leprince P, Nataf P, et al. Pacemaker infective endocarditis. *Am J Cardiol.* 1998;82:480-484.

7. Molina JE. Undertreatment and overtreatment of patients with infected antiarrhythmic implantable devices. *Ann Thorac Surg.* 1997;63:504-509.

8. Choo MH, Holmes DR Jr, Gersh BJ, et al. Permanent pacemaker infections: characterization and management. *Am J Cardiol.* 1981;48:559-564.

9. Chamis AL, Peterson GE, Cabell CH, et al. Staphylococcus aureus bacteremia in patients with permanent pacemakers or implantable cardioverter-defibrillators. *Circulation.* 2001;104:1029-1033.

10. Chua JD, Wilkoff BL, Lee I, Juratli N, Longworth DL, Gordon SM. Diagnosis and management of infections involving implantable electrophysiologic cardiac devices. *Ann Intern Med.* 2000;133:604-608.

11. Baddour LM, Bettmann MA, Bolger AF, et al. Nonvalvular cardiovascular device-related infections. *Circulation.* 2003;108:2015-2031.

12. Klug D, Lacroix D, Savoye C, et al. Systemic infection related to endocarditis on pacemaker leads: clinical presentation and management. *Circulation.* 1997; 95:2098-2107.

13. Lee ME, Chaux A, Matloff JM. Avulsion of a tricuspid valve leaflet during traction on an infected, entrapped endocardial pacemaker electrode: the role of electrode design. *J Thorac Cardiovasc Surg.* 1977;74:433-435.

14. Bower JH, Maraganore DM, McDonnell SK, Rocca WA. Incidence and distribution of parkinsonism in Olmsted County, Minnesota, 1976-1990. *Neurology.* 1999; 52:1214-1220.

15. Melton LJ III. History of the Rochester Epidemiology Project. *Mayo Clin Proc.* 1996;71:266-274.

16. World Health Organization. *International Classification of Diseases, Ninth Revision (ICD-9).* Geneva, Switzerland: World Health Organization; 1977.

17. Duval X, Selton-Suty C, Alla F, et al. Endocarditis in patients with a permanent pacemaker: a 1-year epidemiological survey on infective endocarditis due to valvular and/or pacemaker infection. *Clin Infect Dis.* 2004;39:68-74.

18. Durack DT, Lukes AS, Bright DK; Duke Endocarditis Service. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. *Am J Med.* 1994;96:200-209.

19. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis.* 2000;30:633-638.

20. Bates DW, Goldman L, Lee TH. Contaminant blood cultures and resource utilization: the true consequences of false-positive results. *JAMA.* 1991;265:365-369.

21. Aronson MD, Bor DH. Blood cultures. *Ann Intern Med.* 1987;106:246-253.

22. MacGregor RR, Beaty HN. Evaluation of positive blood cultures: guidelines for early differentiation of contaminated from valid positive cultures. *Arch Intern Med.* 1972;130:84-87.

23. Weinstein MP, Murphy JR, Reller LB, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults, II: clinical observations, with special reference to factors influencing prognosis. *Rev Infect Dis.* 1983;5:54-70.

24. Bekeris LG, Tworek JA, Walsh MK, Valenstein PN. Trends in blood culture contamination: a College of American Pathologists Q-Tracks study of 356 institutions. *Arch Pathol Lab Med.* 2005;129:1222-1225.

25. Friedman ND, Kaye KS, Stout JE, et al. Health care–associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. *Ann Intern Med.* 2002;137:791-797.

26. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with *ICD-9-CM* administrative databases. *J Clin Epidemiol.* 1992;45:613-619.

27. Sohail MR, Khan AH, Friedman PA, et al. Risk factors for electrophysiologic cardiac device infections: a case control study. Paper presented at: 43rd Annual Meeting of the Infectious Disease Society of America; October 6-9, 2005; San Francisco, Calif. Abstract 343.

28. Uslan DZ, Sohail MR, Friedman PA, et al. Frequency of permanent pacemaker or implantable cardioverter-defibrillator infection in patients with gram-negative bacteremia. *Clin Infect Dis.* 2006;43:731-736.

29. Darouiche RO. Device-associated infections: a macroproblem that starts with microadherence. *Clin Infect Dis.* 2001;33:1567-1572.

30. Klug D, Wallet F, Kacet S, Courcol RJ. Involvement of adherence and adhesion *staphylococcus epidermidis* genes in pacemaker lead-associated infections. *J Clin Microbiol.* 2003;41:3348-3350.

31. Gould K, Ramirez-Ronda CH, Holmes RK, Sanford JP. Adherence of bacteria to heart valves in vitro. *J Clin Invest.* 1975;56:1364-1370.

32. Al-Khatib SM, Lucas FL, Jollis JG, Malenka DJ, Wennberg DE. The relation between patients' outcomes and the volume of cardioverter-defibrillator implantation procedures performed by physicians treating Medicare beneficiaries. *J Am Coll Cardiol.* 2005;46:1536-1540.

33. Gould PA, Krahn AD. Complications associated with implantable cardioverter-defibrillator replacement in response to device advisories. *JAMA.* 2006;295:1907-1911.