

Management and Outcome of Permanent Pacemaker and Implantable Cardioverter-Defibrillator Infections

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Objectives

We describe the management and outcome of permanent pacemaker (PPM) and implantable cardioverter-defibrillator (ICD) infections in a large cohort of patients seen at a tertiary care facility with expertise in device lead extraction.

Background

Infection is a serious complication of PPM and ICD implantation. Optimal care of patients with these cardiac device infections (CDI) is not well defined.

Methods

A retrospective review of all patients with CDI admitted to Mayo Clinic Rochester between January 1, 1991, and December 31, 2003, was conducted. Demographic and clinical data were collected, and descriptive analysis was performed.

Results

A total of 189 patients met the criteria for CDI (138 PPM, 51 ICD). The median age of the patients was 71.2 years. Generator pocket infection (69%) and device-related endocarditis (23%) were the most common clinical presentations. Coagulase-negative staphylococci and *Staphylococcus aureus*, in 42% and 29% of cases, respectively, were the leading pathogens for CDI. Most patients (98%) underwent complete device removal. Duration of antibiotic therapy after device removal was based on clinical presentation and causative organism (median duration of 18 days for pocket infection vs. 28 days for endocarditis; 28 days for *S. aureus* infection vs. 14 days for coagulase-negative staphylococci infection [$p < 0.001$]). Median follow-up after hospital discharge was 175 days. Ninety-six percent of patients were cured with both complete device removal and antibiotic administration.

Conclusions

Cure of CDI is achievable in the large majority of patients treated with an aggressive approach of combined antimicrobial treatment and complete device removal. Based on findings of our large retrospective institutional survey and previously published data, we submit proposed management guidelines of CDI. (J Am Coll Cardiol 2007;49:1851-9) © 2007 by the American College of Cardiology Foundation

With an increasing number of indications for use of permanent pacemakers (PPM) and implantable cardioverter-defibrillators (ICD), there has been an accelerated rate of device implantation (1,2). According to one estimate in the U.S., there was a 42% increase in the implantation rate of cardiac devices among Medicare beneficiaries from 1990 to 1999 (3). This was associated with a 124% increase in the rate of cardiac device infection (CDI) among the study population.

Management of CDI is a difficult challenge for both cardiology and infectious diseases specialists. Reported incidence rates of CDI range from 0.13% to 19.9% and 0.0% to 0.8% for PPMs and ICDs, respectively (4-9). A CDI can present with a pulse-generator pocket infection or bloodstream infection (BSI) with or without device-related endocarditis. A CDI is complicated by increased morbidity, mortality, and financial cost (10). Reported mortality rates

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Medical; is on the medical advisory board of Guidant; and is a steering committee member of Medtronic. Dr. Friedman received honoraria from or is a consultant for Medtronic, Guidant, and AstraZeneca; sponsored research from Medtronic, AstraZeneca via Beth Israel, Guidant, St. Jude, and Bard; and holds intellectual property rights with Bard EP, Hewlett Packard, and Medical Positioning, Inc. Dr. Baddour received royalty payments from Elsevier and UpToDate and is an ACP/PIER editorial consultant. Data presented in part at the 43rd Annual Meeting of the Infectious Diseases Society of America, October 6 to 9, 2005, San Francisco, California (abstract no. 387).

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Abbreviations and Acronyms

BSI = blood stream infection
CDI = cardiac device infection
CoNS = coagulase-negative staphylococci
ICD = implantable cardioverter-defibrillator
PPM = permanent pacemaker

of cardiac device-related endocarditis range from 31% to 66% if the infected device is not removed, and 18% or less with a combined management approach with complete device removal and antimicrobial therapy (11,12). Estimated average cost of combined medical and surgical treatment of an infected device ranges from \$25,000 to \$50,000 for PPM and ICD, respectively (13,14). Life-threatening complications of device removal are

well-reported (12,15,16).

To characterize the management and outcome of CDI, we retrospectively reviewed 189 cases of CDI that presented to Mayo Clinic Rochester between January 1991 and December 2003.

Methods

We performed a retrospective review of the medical records of patients with CDI treated at Mayo Clinic Rochester between January 1, 1991, and December 31, 2003. The CDI cases were identified using several Mayo Clinic resources that included the Cardiology Device Database, the Surgical Index, and the computerized central diagnostic index. All patients had consented to use of their medical records for research purposes. The study proposal was approved by the Mayo Foundation Institutional Review Board.

Definitions. A CDI was defined as previously described by our group and others (17-19). Clinical evidence of CDI included local signs of inflammation at the generator pocket, including erythema, warmth, fluctuance, wound dehiscence, erosion, tenderness, or purulent drainage. Presence of PPM/ICD-related endocarditis was clinically confirmed when valvular or lead vegetations were detected by echocardiography, or if the Duke criteria for infective endocarditis were met (12,20). Vegetation was defined as an oscillating intracardiac mass on the electrode leads, cardiac valve leaflets, or endocardial surface in the setting of valve or lead infection confirmed by imaging in more than 1 echocardiographic plane, and positive blood and/or lead tip cultures (12,21-24).

A CDI was microbiologically confirmed based on positive cultures from the generator pocket, lead(s), or blood (in the presence of local inflammatory signs at generator pocket or absence of another source of bacteremia and resolution of blood stream infection after device explantation). Relapse was defined as the recurrence of the device infection with same organism, based on similar antibiogram.

Follow-up. Patients who presented with CDI and underwent device replacement procedure as part of their CDI treatment at Mayo Clinic Rochester had the option of being

followed up at our institution or by their local health care providers. Of the 182 patients who survived index hospitalization for CDI, 142 patients (78%) chose follow-up at our institution, whereas 40 (22%) patients had subsequent care by their referring physician after discharge from Mayo Clinic. Median follow-up duration for cases of CDI was 175 days (mean 657 days).

Statistical evaluation. The Fisher exact test was used to test for differences in proportions for categorical data, and the Wilcoxon rank-sum test was used to test for differences in medians for continuous data. All p values were 2-sided with a level of ≤ 0.05 considered statistically significant. No adjustments for multiple comparisons were made. All analyses were performed using SAS version 8.2 software (SAS Institute Inc., Cary, North Carolina).

Results

Baseline characteristics. A total of 189 cases of CDI met the case definition and were included in the study. Demographic and clinical characteristics of study subjects are summarized in Table 1. The median age of patients was 71.2 years (range 17 to 95 years). Seventy-eight percent were male. Devices included 138 PPMs and 51 ICDs. Most patients (75%) had dual-chamber devices. Fifty-eight (31%) patients had their cardiac devices implanted at Mayo Clinic Rochester, and 131 (69%) had device placement at another institution. Transvenous lead placement (93%) was the most commonly used lead insertion technique. The pulse generator was placed in the pectoral area in 172 (91%) patients and in the abdominal wall in 17 (9%) patients. Indications for initial device placement included heart block (38%), sinus node dysfunction (27%), and ventricular arrhythmias (21%). A CDI occurred after initial device implantation in 79 (42%) patients and after a revision (i.e., system upgrade, lead revision, or generator exchange, and so on) in 110 (58%).

Clinical presentation. Median time from device implantation to infection was 415 days for PPM and 125 days for ICDs ($p = 0.009$). Eighty-six (46%) patients initially presented to Mayo Clinic Rochester, and 103 (54%) were referred to Mayo Clinic Rochester because of lack of available expertise for lead extraction at the referring facility. Pocket infection, with (17%) or without (52%) BSI, was the most common clinical presentation, followed by device-related endocarditis (23%). Most patients had localized inflammatory signs at the pocket site (Table 2). Systemic signs of sepsis were present in less than one-half of the cases. Ten (5%) cases presented with erosion of lead or device generator, without accompanying inflammatory signs at the generator pocket site.

Microbiology. Coagulase-negative staphylococci (CoNS, 42%) and *Staphylococcus aureus* (29%) were the most common causes of CDI, followed by gram-negative bacilli (9%), including *Klebsiella pneumoniae*, *Serratia marcescens*, *Pseudo-*

monas aeruginosa, *Stenotrophomonas maltophilia*, *Acinetobacter xylosoxidans*, *Acinetobacter baumannii*, *Citrobacter koseri*, *Morganella morganii*, *Hemophilus influenzae*, and *Moraxella catarrhalis* (Fig. 1). Two patients had fungal (*Candida albicans* and *Aspergillus fumigatus*) infection. Polymicrobial infection was present in 7% of cases. Fourteen (7%) patients had localized inflammatory signs at generator pocket or erosion of device/lead but pocket cultures were negative. Purulent material was encountered (intraoperative) within the pulse-generator pocket in 151 (80%) of the cases (11% of these patients had no inflammatory signs at the generator pocket on physical examination). Seventy-five percent of the

Table 1

Demographic and Clinical Characteristics of Patients With CDI Who Were Treated at Mayo Clinic Rochester Between 1991 and 2003 (n = 189)

Characteristic	Value
Age (yrs), median (range)	71 (17-95)
Gender, male	148 (78%)
Device	
PPM	138 (73%)
ICD	51 (27%)
Chambers	
Single	44 (23%)
Dual	142 (75%)
Lead placement	
Transvenous	176 (93%)
Epicardial	5 (3%)
Both	8 (4%)
Indication	
Heart block	71 (38%)
Sinus node dysfunction	51 (27%)
Ventricular tachycardia/fibrillation	39 (21%)
Other	28 (14%)
Last procedure before CDI	
De novo implantation	79 (42%)
System revision/upgrade	41 (22%)
Lead revision/insertion	19 (10%)
Generator replacement	49 (26%)
Time from implant/last intervention to infection, median days (mean)	
PPM	415 (920)
ICD	125 (399)
Comorbid conditions	
Coronary artery disease	114 (60%)
Heart failure	96 (51%)
Anticoagulation	67 (35%)
Diabetes mellitus	46 (24%)
Chronic obstructive pulmonary disease	34 (18%)
Malignancy	24 (13%)
Clinical presentation	
Pocket infection	99 (52%)
Pocket infection with bacteremia	32 (17%)
Device-related endocarditis	44 (23%)
Bacteremia without localizing signs at pocket	21 (11%)
Generator or lead erosion	10 (5%)

CDI = cardiac device infection; ICD = implantable cardioverter-defibrillator; PPM = permanent pacemaker.

Table 2 Clinical Presentation of Patients With CDI (n = 189)

Presenting Signs/Symptoms	n (%)
Systemic symptoms	
Fever (>38°C)	82 (43)
Chills	73 (39)
Malaise	79 (42)
Anorexia	32 (17)
Nausea	16 (8)
Sweating	34 (18)
Hypotension (systolic blood pressure <90 mm Hg)	18 (10)
Murmur on examination	66 (35)
Symptomatic heart failure	52 (28)
Local findings at generator site	
Erythema	128 (68)
Pain	93 (49)
Swelling	127 (67)
Warmth	71 (38)
Tenderness	86 (46)
Drainage	95 (50)
Purulent drainage	65 (34)
Skin ulceration	59 (31)
Generator/lead erosion	48 (25)
Intraoperative purulence at generator pocket	151 (80)
Laboratory abnormalities	
Leukocytosis (WBC >10 × 10 ⁹ /l), n = 188	82 (43)
Anemia (HCT <38% in men and <35% in women), n = 188	94 (50)
High erythrocyte sedimentation rate (ESR >22 mm/h in men and >29 mm/h in women), n = 76	47 (25)
Positive blood culture (n = 188)	76 (40)

CDI = cardiac device infection; ESR = erythrocyte sedimentation rate; HCT = hematocrit; WBC = white blood cell count.

above cases had positive cultures from the generator pocket. Blood cultures were positive in only 76 (40%) of all cases. **Complications of device infection.** Complications of CDI included septic arthritis (n = 6), vertebral osteomyelitis (n = 2), sternal osteomyelitis (n = 2), femoral osteomyelitis (n = 1), lung abscesses (n = 5), splenic abscess (n = 1),

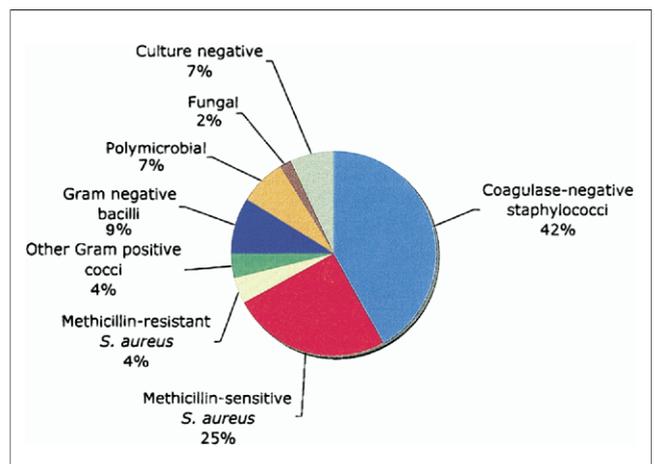


Figure 1 Microbiology of PPM/ICD Infections (n = 189)

ICD = implantable cardioverter-defibrillator; PPM = permanent pacemaker.

brain abscess (n = 1), liver abscess (n = 1), and perinephric abscess (n = 1). Twenty-two (11.6%) patients had thrombosis of a vein where leads were in place (subclavian vein or superior vena cava), and in 6 of these cases, they presented with symptomatic pulmonary embolism. The majority of patients (n = 147, 78%) had an echocardiogram (transthoracic or transesophageal) performed, and 44 (23%) had either lead and/or valvular vegetations. The diameter of vegetations ranged from 0.3 to 7.0 cm in the longest dimension. It is noteworthy that none of these patients developed clinical manifestations of pulmonary embolism as a complication of percutaneous lead extraction.

Explantation of infected devices. The cardiac device was explanted in 182 (96%) patients at the time of initial presentation. Three (2%) other patients suffered relapsing CDI and had explantation after failure of conservative (medical) treatment. A cardiac device was not explanted in 4 patients because of high operative risk (advanced age and decompensated heart failure with ejection fraction $\leq 20\%$). The entire device system was explanted in 178 (94%) patients, whereas lead extraction was unsuccessful in 7 (4%) cases. Most patients (90%) underwent percutaneous lead extraction with use of manual traction (15%), locking stylet (34%), or laser sheath (41%). Nineteen patients (10%) had lead extraction via median sternotomy.

Complications of lead extraction. Twenty patients suffered complications of percutaneous lead extraction (3 manual traction, 7 locking stylet, and 10 cases with laser

sheaths), which included damage to the tricuspid valve (n = 3) that required valve annuloplasty in 2 patients, subclavian vein laceration (n = 3), hemothorax (n = 4), pocket hematoma (n = 3), fracture of lead tip requiring surgical intervention (n = 6), and massive hemorrhage that required surgical intervention (n = 5) and resulted in the death of 1 patient. Surgical removal of epicardial leads was complicated by massive hemorrhage (n = 2) that was lethal in 1 patient, postoperative cardiac arrest requiring intensive care unit stay (n = 1), subclavian vein laceration (n = 1), and ventriculotomy requiring operative repair (n = 1). Complications during lead extraction were more common in patients with history of multiple device-related procedures (13 of 87, 14.9%) compared with those with initial implants (7 of 77, 9.1%). However, this difference was not statistically significant (p = 0.25).

Antimicrobial treatment. All patients received antimicrobials after removal or debridement of infected device system. Most patients received at least 2 weeks of antibiotics after removal of an infected device (Fig. 2). Median duration of antibiotic treatment was significantly longer in patients with *S. aureus* infection as compared to those with CoNS (28 days vs. 14 days, p < 0.001). Patients with device-related endocarditis (valvular or lead vegetation) and BSI received a median of 28 days of antibiotics after device removal. Cases with ICD infection had a longer duration of antibiotics (median 22 days) as compared to those with PPM infection (median 16 days), but this difference was not statistically

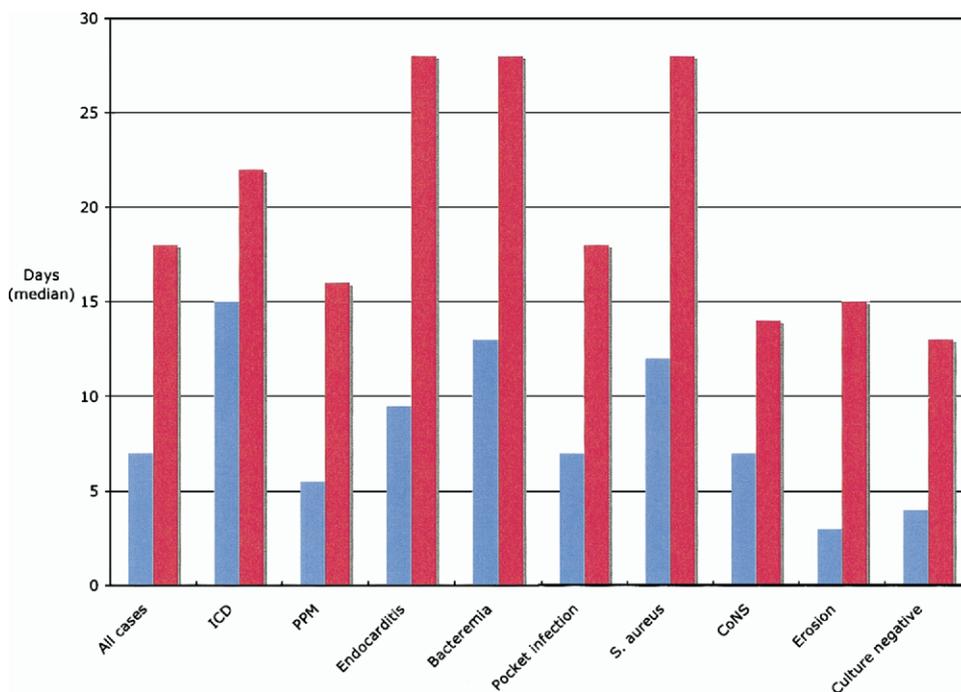


Figure 2 Timing of Reimplantation of New Cardiac Device and Duration of Postexplant Antibiotic Treatment

Blue bars = time from explant to reimplant; red bars = post-explant antibiotic duration. CoNS = coagulase-negative staphylococci; other abbreviations as in Figure 1.

significant ($p = 0.27$). Most patients (97%) received a combination of intravenous and oral antibiotics. Only 3% were treated with oral antibiotics alone. Adverse effects of antibiotic treatment included diarrhea (8%), nephrotoxicity (5%), neutropenia (2%), *Clostridium difficile* colitis (1%), and oral candidiasis (1%).

Reimplantation of a new device. All patients were assessed for ongoing need of a cardiac device after extraction of an infected system. Reimplantation of a new device was considered necessary in only 127 (67%) of the cases. Median time from explantation to reimplantation was significantly longer for patients with BSI compared with nonbacteremic cases (13 days vs. 7 days, $p < 0.0001$). A new system was placed as early as 3 days in cases of negative blood cultures (Fig. 2). The median time from explantation to reimplantation in patients with CoNS was 7 days compared with a delay of 12 days in cases of *S. aureus* infection ($p = 0.09$). In cases in which a new device system was implanted, most patients (94%) had transvenous lead insertion with implantation of a generator on the opposite side of the infected pocket. Epicardial electrodes were placed in 7 (5%) patients.

Generator or lead erosion. Among our study subjects with CDI, 10 patients presented with generator or lead erosion only. Despite the absence of local inflammatory signs at the pocket site, purulent material in the pulse-generator pocket was noted intraoperatively in 3 (30%) of these cases, and 9 (90%) had positive cultures from an intraoperative swab of the pocket. The causative micro-organism for CDI in this group of patients included common skin flora such as CoNS ($n = 4$), *S. aureus* ($n = 3$), and *Propionibacterium* spp. ($n = 1$), whereas 1 patient had polymicrobial infection with CoNS, *Propionibacterium* spp., and *Corynebacterium* spp. All patients had explanation of the infected device at the initial presentation (complete hardware successfully removed in 9 cases, whereas percutaneous lead extraction was unsuccessful in 1 case). Median time from removal of an infected device to insertion of a new system was 3 days. Among cases ($n = 7$) with no intraoperative evidence of purulence in the generator pocket, 4 (57%) had a new system placed on the same day when the infected device was removed. All patients were cured and none had infection relapse at their last follow-up visit (mean duration 78 weeks).

Outcome. The average duration of hospitalization for CDI was 17 days (median 13 days). Seven patients died during index hospitalization for CDI. Of the remaining 182 cases, follow-up data were available for 142 cases (40 patients were followed up elsewhere). Most patients (135, 95%) remained free of infection, after the initial treatment, at the last follow-up (median follow-up duration 175 days; mean 657 days). Two patients had persistent pocket infection caused by retained hardware. Five cases presented with relapse of infection. Clinical characteristics, microbiology, management, and outcome of these 5 cases are summarized in Table 3. Two of these patients were subsequently cured with complete removal of the infected device.

Table 3 Characteristics of Patients With Relapse of CDI

Case	Device	Comorbid Conditions	Presentation	Microorganism	Initial Hardware Removal	Reinserted New Device	Timing of Relapse (weeks)	Relapse/Outcome
1	ICD (TVL + EPL)	DM, CHF	Pocket + BSI	CoNS	Partial*	No	6	EPL surgically removed at relapse. However, patient died of stroke.
2	ICD (TVL + EPL)	CHF	Pocket infection	MSSA	Partial†	Yes	4	Relapsed with device-related TV endocarditis. Cured with removal of epicardial patches.
3	ICD (EPL)	CHF	Pocket + BSI	CoNS	Partial*	Yes	16	Persistent pocket infection at last follow-up.
4	PPM (TVL)	Liver TX, Hodgkins lymphoma, HD, CHF	Endocarditis	MRSA	Complete	Yes‡	12	Died of MRSA sepsis and small bowel perforation despite removal of new device.
5	PPM (TVL)	CHF	Endocarditis	CoNS	Complete	Yes§	24	Cured with removal of replacement device.

*Patient had abandoned EPL from previous devices, which were not removed because of high operative risk. †Epicardial patches were difficult to remove at initial surgery and were left behind. ‡Patient had dialysis catheter-related MRSA bacteremia with seeding of new device. §Temporary pacing wires before insertion of new device. ¶BSI = bloodstream infection; CHF = congestive heart failure; CoNS = coagulase-negative staphylococci; DM = diabetes mellitus; EPL = epicardial leads; HD = hemodialysis; ICD = implantable cardioverter-defibrillator; MRSA = methicillin-resistant *S. aureus*; MSSA = methicillin-sensitive *S. aureus*; PPM = permanent pacemaker; TV = tricuspid valve; TVL = transvenous leads; TX = transplant.

There were 9 in-hospital deaths, 7 during index hospitalization and 2 in patients who were subsequently hospitalized for relapse of infection. Five of these patients had device-related endocarditis (4 with staphylococci and 1 with *Aspergillus fumigatus*). Staphylococcal BSI with sepsis (n = 5) was the most common cause of death. Two patients died secondary to complications of device extraction surgery. One patient died of ventilator-associated pneumonia during an intensive care unit stay after device removal. One severely immunocompromised patient with device-related fungal endocarditis and metastatic abscesses died.

Seven patients had partial device explantation at initial presentation. Two were lost to follow-up after the index hospitalization (both cases had abandoned epicardial leads from previous devices, and the currently infected devices had transvenous leads that were removed along with generators). One patient died of surgical complications during a second attempt at complete hardware removal. Of the remaining 4 patients, 2 had a relapse (Table 3, cases 2 and 3). The other 2 patients remained infection-free despite only partial device removal. Both had negative blood cultures and no evidence of endocarditis on echocardiography. Percutaneous lead extraction was attempted but was unsuccessful in first patient with pocket infection. Transvenous lead removal was not attempted in the second case because of absence of inflammatory changes during generator pocket exploration. In both cases, there was no evidence of infection at their last follow-up visit (5 months in the case of pocket infection and 4 years in the case of generator erosion only).

Discussion

Despite improvements in the design and implantation techniques, infection of the cardiac devices remains a serious problem. The current study is one of the largest reported series of CDI in the United States and the only one to propose management guidelines.

Clinical presentation and microbiology. There was considerable variation in time from device implantation to onset of infection in our survey. Median time from implantation to infection was shorter for ICDs (125 days) than for PPMs (414 days). This time difference between the 2 groups may in part be caused by an increased proportion of *S. aureus* infection in patients with an ICD (35%) as compared to those with PPM (26%). Patients with PPM infection were more likely to have CoNS isolated (46%) from blood or pocket cultures than those with an ICD (31%).

Most patients with CDI present with only localized inflammatory signs at the generator pocket (Table 2), and a lack of systemic signs should not sway clinicians away from a suspicion of CDI (19). Nonspecific laboratory abnormalities such as leukocytosis, anemia, and high sedimentation rate were present in less than one-half of the cases in the current study. Staphylococcal species account for more than two-thirds of CDI cases in most published series (11,12,15,19,25) and were predominant in the present inves-

tigation (Fig. 1). Therefore, empiric antibiotics for suspected CDI should include coverage for staphylococci while awaiting microbiology results.

Conservative treatment versus complete device removal. Some investigators have advocated conservative treatment with antibiotics and generator pocket debridement without hardware removal (26-28). Most previously published studies, however, have shown unacceptably high failure rates with conservative treatment (11-13,19,22,23,29-35).

The Heart Rhythm Society guidelines state that extraction of an entire lead may not be necessary if the lead can be cut through a sterile incision, totally separate from an infected pocket (36). However, the intracardiac portion of a lead may be colonized in cases in which CDI findings are limited to the pulse-generator pocket only (13,25,37), and there is a high risk of treatment failure with a lead-retention approach as recommended by the Heart Rhythm Society (25,34,38-41). In the current study, 5 patients had CDI relapse (2.6%), and 3 of them had only partial explantation of the device (generator only) at initial presentation. The other 2 patients had a temporary pacing wire as a bridge between explantation of an infected device and reimplantation of a new device. Use of the temporary pacing wires has been identified as a risk factor for subsequent CDI in 2 recent studies (42,43). Based on the above findings, we recommend complete hardware removal to achieve CDI cure; this mirrors the recommendations of the American Heart Association (4).

Percutaneous versus surgical lead extraction. Extraction of cardiac device leads is not without risk (16,31,40). Despite advances in techniques for percutaneous lead extraction (44), there is still considerable morbidity and mortality associated with this procedure. In our study, 20 patients (11%) had complications of percutaneous lead extraction that included damage to cardiac valves, venous lacerations, bleeding complications, and lead tip fracture that required surgical intervention. Some investigators have expressed concern about transvenous lead removal when lead vegetation size is >1 cm because of the risk of pulmonary embolization of lead vegetation fragments (12,45-47). No patient had a clinically significant pulmonary embolism in our series despite the presence of vegetation sizes that ranged from 0.3 to 7.0 cm in the longest dimension. Others have reported similar experiences (22,23,48,49). Lead removal by cardiectomy (50,51) has been advocated to prevent symptomatic pulmonary embolism but, as shown in the current case series, this approach can be complicated by serious adverse events. Five patients suffered massive hemorrhages postoperatively, and 1 died in our series.

Duration of antimicrobial treatment. The duration of antimicrobial treatment for CDI depended on the clinical presentation and the causative agent. In a large case series from the Cleveland Clinic Foundation (19), the median duration of antibiotic treatment in CDI cases with pocket infection and those with bacteremia was 26 days and 41 days, respectively. However, in our practice, cases of CDI with only pocket

infection were treated with 10 to 14 days of antimicrobials and those with BSI for 4 weeks after device removal. Similarly, patients with cardiac device-related endocarditis limited to the right heart can be treated with 4 weeks of antibiotics instead of the 6-week treatment course that has been advocated by some (12,13,19). Infection by certain microorganisms may require longer antimicrobial treatment for complete eradication of a CDI. In our study, cases of CDI attributable to *S. aureus* had

significantly longer treatment after device explantation as compared to those with CoNS infection (28 days vs. 14 days, $p < 0.001$). An *S. aureus* CDI is also associated with a higher mortality rate as compared with that caused by other pathogens. In our study, there were 9 in-hospital deaths (crude mortality rate 4.7%), and 5 had *S. aureus* identified in blood cultures.

Timing and need of a replacement device. Timing of reimplantation of a new device system after extraction of

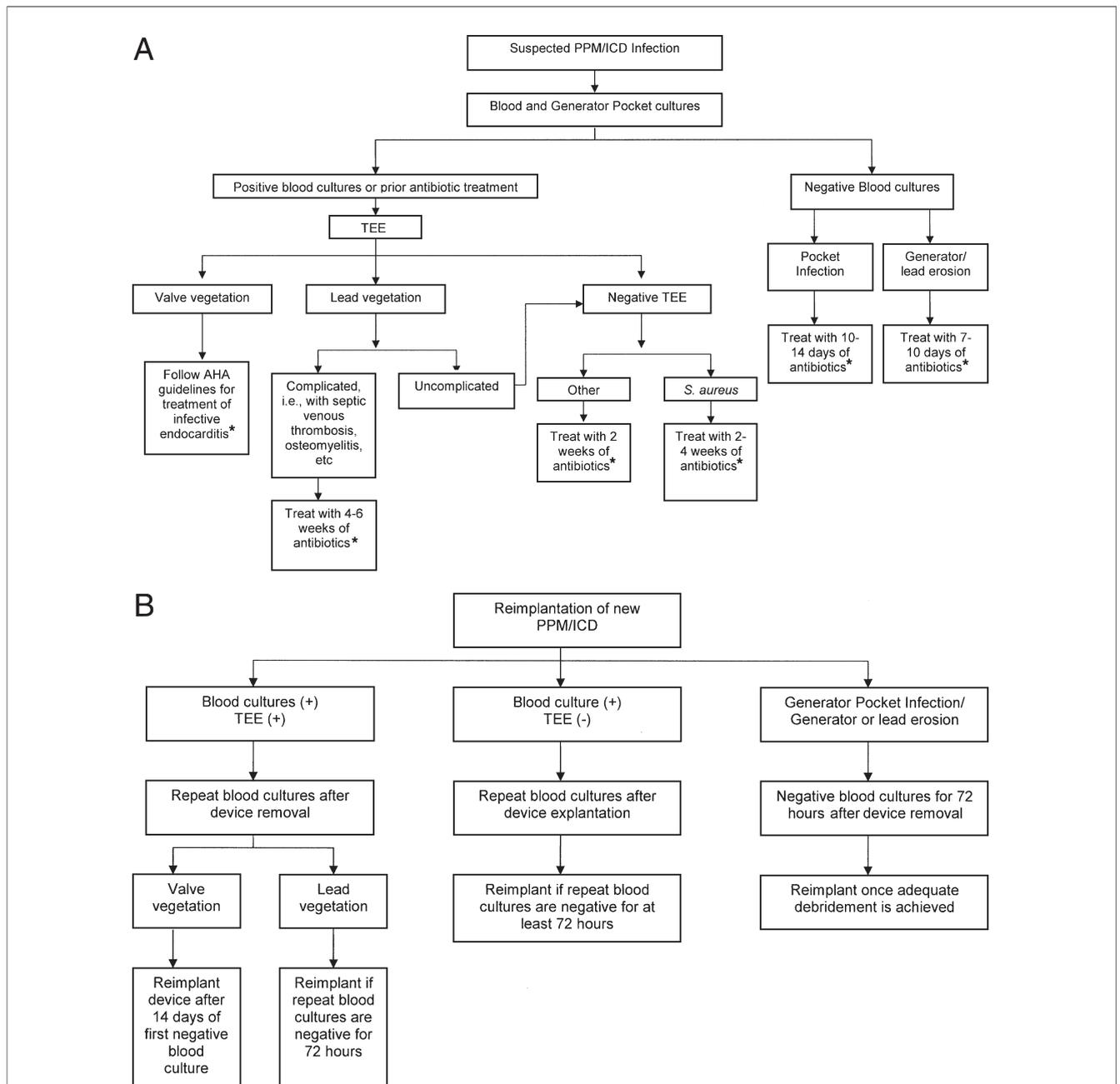


Figure 3 Mayo Clinic Algorithm of Cardiac Device Infection Management

(A) Approach to management of adults with PPM/ICD infection (also see Table 4). This algorithm applies only to the patients with complete device explantation. *Duration of antibiotics should be counted from the day of device explantation. (B) Guidelines for reimplantation of new device in patients with PPM/ICD infection (see also Table 4). AHA = American Heart Association; TEE = transesophageal echocardiography; other abbreviations as in Figure 1.

Table 4 Mayo Clinic Guidelines for the Diagnosis and Management of Cardiac Device Infections

1. All patients should have at least 2 sets of blood cultures drawn at initial evaluation.
2. Generator tissue Gram stain and culture and lead tip culture should be obtained.
3. Patients who either have positive blood cultures or have negative blood cultures but had recent antibiotics before obtaining blood cultures should have a transesophageal echocardiogram (TEE) to assess for device-related endocarditis.
4. Sensitivity of TTE is low and is not recommended to evaluate for device-related endocarditis.
5. Patients with negative blood cultures and recent prior antibiotics and valve vegetations on TEE should be managed in consultation with an infectious diseases expert.
6. All patients with device infection should undergo complete device removal, regardless of clinical presentation.
7. A large (>1 cm) lead vegetation is not a stand alone indication for surgical lead removal.
8. Blood cultures should be repeated in all patients after device explantation. Patients with persistently positive blood cultures should be treated for at least 4 weeks with antimicrobials even if TEE is negative for vegetations or other evidence of infection.
9. Duration of antimicrobial therapy should also be extended to ≥ 4 weeks in patients with complicated infection (endocarditis, septic venous thrombosis, osteomyelitis, metastatic seeding).
10. Adequate debridement and control of infection should be achieved at all sites before reimplantation of a new device.
11. Reevaluation for continued need of the device should be performed before new device placement.
12. If an infected cardiac device cannot be removed, than long-term suppressive antibiotic therapy should be administered after completing an initial course of treatment and securing a clinical response to therapy. Infectious diseases expert opinion should be sought.

an infected device remains a subject of debate and is influenced by the causative agent and clinical presentation of CDI. Median time from explantation to reimplantation of a new device was significantly longer for patients with BSI as compared to those with negative blood cultures (13 days vs. 7 days, $p < 0.0001$) in the current investigation. There was no statistically significant difference in time from explant to reimplant in patients with CoNS infection (median 7 days) as compared to those with *S. aureus* infection (median 12 days, $p = 0.09$). Although some investigators (13) have suggested delaying reimplantation of new device for 10 to 14 days in cases of pocket infection (without BSI) and up to 6 weeks in bacteremic patients, our data suggest that devices can be safely reimplanted once the pocket has been adequately debrided and blood cultures are negative. These data are consistent with previously published reports (19). Moreover, maintaining a transvenous temporary device increases the risk of subsequent CDI (43,52) and cannot be used indefinitely.

The need for placement of a new device system should be carefully assessed in all patients with CDI because an appreciable number of patients may not require a subsequent cardiac device. Discontinuation of electrophysiologic device use after removal of an infected system has been reported in 13% to 52% of cases (11,19,30,53). In our study, reimplantation of a new device was not required in one-third of patients.

Proposed Mayo Clinic guidelines for management of CDI. Based on the findings of our retrospective analysis and review of published literature (1-53), we propose guidelines for CDI (Figs. 3A and 3B, Table 4) to assist clinicians in patient management. These recommendations are not meant to replace individual patient management, however, and consultation with available specialists is advocated.

Study limitations. Our investigation has several limitations. First, retrospective studies have inherent limitations, such as potential selection and recall biases. Second, Mayo

Clinic Rochester is a tertiary referral center with referral bias, as was shown in the current survey. Patients who are referred to a specialized cardiovascular center may be sicker and have more complex cardiac devices than the general population. Third, the majority of our cohort was white (91%), and this reflected both local population demographics and the referral population. Despite these limitations, data presented herein provide critical information to clinicians who manage CDI.

Conclusions. A CDI is an important and serious complication of device use. Because of the expected continued increase in the number of cases of CDI and the current lack of prospective, randomized trial data to assist in defining optimal treatment, we present proposed guidelines to assist clinicians in the management of CDI.

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