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ORIGINAL ARTICLE

Infective Endocarditis Complicating Permanent Pacemaker and Implantable Cardioverter-Defibrillator Infection

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OBJECTIVE: **To describe management of patients with permanent pacemaker (PPM)– and implantable cardioverter-defibrillator (ICD)–related endocarditis.**

PATIENTS AND METHODS: **We retrospectively reviewed all cases of infection involving PPMs and ICDs among patients presenting to Mayo Clinic's site in Rochester, MN, between January 1, 1991, and December 31, 2003. Cardiac device–related infective endocarditis (CDIE) was defined as the presence of both vegetation on a device lead or valve and clinical or microbiological evidence of CDIE. Of 189 patients with PPM or ICD infection who were admitted during the study period, 44 met the case definition for CDIE (33 PPM, 11 ICD).**

RESULTS: **The mean ± SD age of patients was 67±14 years. Staphylococci (36 [82%]) were the most commonly isolated pathogens. Nearly all patients (43 [98%]) were treated with a combined approach of complete hardware removal and parenteral antibiotics. The median duration of antibiotic treatment after infected device explantation was 28 days (interquartile range, 19-42 days). Device leads were removed percutaneously in 34 cases (77%); only 7 cases (16%) required surgical lead extraction. Percutaneous extraction was uncomplicated in 15 patients with lead vegetation greater than 10 mm in diameter. Six patients (14%) died during hospitalization. Twenty-seven (96%) of 28 patients remained infection free at their last visit (median follow-up, 183 days; intraquartile range, 36-628 days).**

CONCLUSION: **Prompt hardware removal and prolonged parenteral antibiotic administration decrease mortality among patients with CDIE. The presence of a large (>10 mm in diameter) vegetation on a lead is not a contraindication for percutaneous lead extraction.**

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CDIE = cardiac device–related infective endocarditis; ICD = implantable cardioverter-defibrillator; IQR = interquartile range; MCR = Mayo Clinic's site at Rochester, MN; PPM = permanent pacemaker; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography

Use of permanent pacemakers (PPMs) and implantable cardioverter-defibrillators (ICDs) for various cardiac rhythm disturbances has rapidly increased in the United States.[1,2] This increase is associated with a rising incidence of infection among patients with implanted cardiac devices.[3,4] The reported rate of infection ranges from 0.13% to 19.9% for PPMs and from 0.7% to 1.2% for ICDs.[5-10] Cardiac device–related infective endocarditis (CDIE) accounts for approximately 10% of all cases of device infection.[11] The condition is associated with substantial morbidity, mortality, and financial cost.[12-14] According to one estimate, the mean hospital cost for treatment of a single PPM or ICD infection was $24,459 and $57,213, respectively.[9]

Data to guide therapy in patients with CDIE are limited. Moreover, the definition of CDIE has varied in previously published reports[11,15,16]; that variation has made it difficult to determine the most appropriate management. The current study is one of the largest case series on CDIE and addresses some controversial issues in its management.

PATIENTS AND METHODS

We retrospectively reviewed medical records of all patients who were treated for infection associated with their cardiac devices at Mayo Clinic's site at Rochester, MN (MCR), between January 1, 1991, and December 31, 2003. Cases of device infection were identified by using several MCR resources that included the Heart Rhythm Services ICD and PPM Databases, the Surgical Index, and the computerized central diagnostic index. Patients who fulfilled the

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criteria for CDIE were included in this analysis. All patients consented to use of their medical records for research purposes. The study proposal was approved by the Mayo Clinic Institutional Review Board.

Definitions

Cardiac device infection was defined as previously described by our group.[14,17-19] Clinical evidence of device infection was local signs of inflammation at the generator pocket, including erythema, warmth, fluctuation, wound dehiscence, erosion, tenderness, or purulent drainage. The diagnosis was clinically confirmed when valvular or lead vegetations were detected by echocardiography or if the Duke criteria for infective endocarditis were met.[13,20,21] A vegetation was defined as an oscillating intracardiac mass on the device leads, cardiac valve leaflets, or endocardial surface, confirmed by imaging in more than 1 echocardiographic plane, in cases of valve or lead infection that were identified by positive blood or lead-tip cultures.[13,16,22-24]

Infection was microbiologically confirmed by positive cultures from the generator pocket, leads, or blood (in the presence of local inflammatory signs at the generator pocket or absence of another source of bacteremia and resolution of bloodstream infection after device explantation). Contamination of blood cultures was defined[25-27] as recovering 1 or more of the following bacteria in only one of a series of blood culture specimens: coagulase-negative staphylococcal species, *Propionibacterium acnes*, *Micrococcus* species, viridans group streptococci, *Corynebacterium* species, or *Bacillus* species.

Statistical Analyses

Categorical measures were summarized by using counts and percentages; continuous measures were summarized by using either means with standard deviations or medians with the 25th and 75th percentiles (interquartile range [IQR]), depending on whether data were skewed. All analyses were performed by using SAS, version 8.2, software (SAS Institute, Cary, NC).

RESULTS

Demographic and Clinical Characteristics

We identified 189 cases of infection in association with cardiac electrophysiologic devices (PPMs or ICDs) among patients admitted to MCR between January 1, 1991, and December 31, 2003. Forty-four (23%) of these cases met the criteria of CDIE (34 definite, 10 probable). Demographic characteristics of these 44 patients are summarized in Table 1.

The mean ± SD age at onset of CDIE was 67±14 years. Most patients (34 [77%]) were male, and 40 (91%) were white. Twelve devices (27%) were placed at MCR, and 32 (73%) were implanted elsewhere. Indications for device placement are summarized in Table 1. Nineteen patients (43%) had initial device implantation before CDIE; the remaining 25 cases (57%) had a device revision procedure before presenting with CDIE. Coronary artery disease (27 [61%]), chronic heart failure (27 [61%]), and diabetes mellitus (13 [30%]) were the most common comorbid conditions.

TABLE 1. **Demographic and Clinical Characteristics of 44 Patients[a] With Cardiac Device–Related Infective Endocarditis[b]**

Characteristic	Value
Age (y) at time of procedure, mean ± SD	
Device implantation	65±15
Onset of infection	67±14
Male	34 (77)
Device	
Permanent pacemaker	33 (75)
Implantable cardioverter-defibrillator	11 (25)
Chambers	
Single	11 (25)
Dual	33 (75)
Pulse-generator location	
Right pectoral	14 (32)
Left pectoral	29 (66)
Abdominal	1 (2)
Transvenous lead placement	44 (100)
Indication	
Heart block	19 (43)
Sinus node dysfunction	10 (23)
Ventricular tachycardia or fibrillation	8 (18)
Syncope	1 (2)
Other	6 (14)
Last procedure before CDIE	
De novo implantation	19 (43)
System revision or upgrade	10 (23)
Lead revision or insertion	5 (11)
Generator replacement	10 (23)
Time (d) from last procedure to CDIE, median (IQR)	419 (55-1186)
Comorbid conditions	
Coronary artery disease	27 (61)
Chronic heart failure	27 (61)
Diabetes mellitus	13 (30)
Anticoagulation	12 (27)
Chronic renal insufficiency	12 (27)
Chronic obstructive pulmonary disease	10 (23)
Malignancy	5 (11)
Autoimmune disease	5 (11)
Hemodialysis	5 (11)

[a] Patients were treated at Mayo Clinic's site in Rochester, MN, between January 1, 1991, and December 31, 2003. CDIE = cardiac device–related infective endocarditis; IQR = interquartile range.
[b] Values are expressed as number (percentage) unless indicated otherwise.

Clinical Presentation

The median duration from device implantation to the development of CDIE was 419 days (IQR, 55-1186 days). Median time from onset of symptoms to hospital admission was 25 days (IQR, 7-70 days). Nineteen patients (43%)

TABLE 2. **Clinical Presentation of 44 Patients With Cardiac Device–Related Infective Endocarditis**

Clinical variable	No. (%)
Systemic symptoms	
Fever (temperature, >38°C)	35 (80)
Chills	33 (75)
Malaise	33 (75)
Anorexia	16 (36)
Nausea	9 (20)
Sweating	14 (32)
Hypotension (systolic blood pressure <90 mm Hg)	9 (20)
Murmur on examination	19 (43)
Symptoms of heart failure	19 (43)
Local findings at pulse-generator site	
Erythema	17 (39)
Pain	17 (39)
Swelling	20 (45)
Warmth	11 (25)
Tenderness	14 (32)
Drainage	11 (25)
Purulent drainage	7 (16)
Skin ulceration	4 (9)
Generator or lead erosion	3 (7)
Intraoperative finding of purulence in the generator pocket	25 (47)
Laboratory abnormalities	
Leukocytosis[a]	26 (59)
Anemia[b]	29 (66)
High erythrocyte sedimentation rate[c]	10/17 (59)[d]
Positive blood culture	34 (77)
Positive swab culture from generator-pocket tissue	23/38 (61)[d]
Positive culture from electrode lead tips	23/29 (79)[d]

[a] White blood cell count >10 × 10^9/L.
[b] Hematocrit <38% in male and <35% in female patients.
[c] Rate >22 mm/h in male and >29 mm/h in female patients.
[d] Data were missing for some patients.

were admitted to MCR directly, whereas 25 patients (57%) were referred from outside institutions for device lead extraction. Clinical presentation for all CDIE cases is summarized in Table 2. Fever (35 patients [80%]), chills (33 [75%]), and malaise (33 [75%]) were the most common presenting symptoms. Twenty-one patients (48%) had inflammatory signs at the generator pocket. Purulent material was noted at the generator pocket during surgery in 25 patients (57%). Four of these 25 patients (16%) had no inflammatory signs at the generator pocket on physical examination. Two-thirds of all cases of CDIE had nonspecific laboratory abnormalities, including leukocytosis, anemia, and a high erythrocyte sedimentation rate (Table 2).

Microbiology

Coagulase-negative staphylococci (18 patients [41%]) and *Staphylococcus aureus* (18 [41%]) were the most common causes of CDIE (Table 3), followed by gram-negative bacilli (2 [5%]) and fungi (2 [5%]). Blood cultures were positive in most cases (34 [77%]) (Table 2). Cultures from generator-pocket tissue and lead tips were positive in 61% and 79% of cases, respectively (Table 2). Of the 10 patients with negative blood cultures, 6 (60%) had received antibiotics before blood cultures were obtained. Positive lead cultures had limited use for establishing a definite diagnosis of CDIE (Figure). Among the 189 patients who were admitted to MCR with a diagnosis of device (PPM or ICD) infection, most with positive lead tip cultures also had clinical evidence of generator-pocket infection and had the same organisms isolated from generator-pocket and lead tip cultures.

Echocardiographic Findings

All patients underwent echocardiography during their index hospitalization (Table 4). All patients had echocardiographic features consistent with vegetation on a device lead or cardiac valve leaflet. Vegetation infection was confirmed by histopathologic or microbiological examination in 6 cases. The tricuspid valve (11 patients [25%]) was the most commonly involved cardiac valve, followed by the aortic (5 [11%]) and mitral (3 [7%]) valves. All 18 cases of valvular vegetations were evident with transesophageal echocardiography (TEE) but were visible with transthoracic echocardiography (TTE) in only 1 case. Similarly, lead vegetations were seen by TTE in 3 patients (7%) and by TEE in 35 (80%). Median diameter of the vegetation was 11 mm (range, 3-70 mm; IQR, 8-20 mm).

Complications of CDIE

Of 8 patients (18%) with metastatic foci of infection, 3 (17%) had osteomyelitis; 3 (17%), septic arthritis; 2 (11%), lung abscess; and 1 (16%), hepatosplenic abscesses. Five patients (11%) had septic pulmonary emboli at admission (diagnosis by computed tomography in 3 cases, ventilation-perfusion scan in 1 case, and chest radiograph in 1 case).

TABLE 3. **Microbiological Distribution of 44 Patients With Cardiac Device–Related Infective Endocarditis**

Microorganism	No. of infections by time from last procedure to endocarditis		
	<12 wk	12 wk-1 y	>1 y
Coagulase-negative staphylococci	6	4	8
Staphylococcus aureus[a]	6	3	9
Gram-negative bacilli[b]	…	…	2
Propionibacterium acnes	1	…	1
Fungal[c]	…	1	2
Polymicrobial	…	…	1

[a] Of the 18 *S aureus* infections, 3 were methicillin-resistant *S aureus* and 15 were methicillin-susceptible *S aureus*.
[b] Of the 2 gram-negative bacilli infections, 1 was *Pseudomonas aeroginosa* and 1 was *Alcaligenes xylosoxidans*.
[c] Of the 3 fungal infections, 1 was *Candida albicans* and 2 were *Aspergillus fumigatus*.

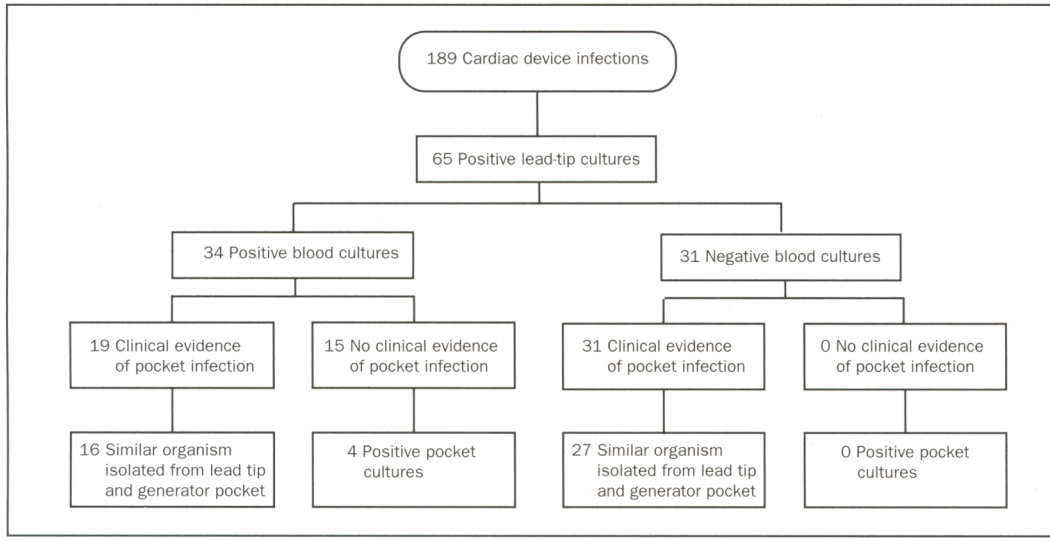

FIGURE. Utility of positive lead cultures as a criterion to establish definite diagnosis of cardiac device–related infective endocarditis in patients with permanent pacemaker or implantable cardioverter-defibrillator infection (total of 189 cases with infection of permanent pacemaker or implantable cardioverter-defibrillator including 44 that met cardiac device–related infective endocarditis case definition). Clinical evidence of pocket infection included presence of erythema, pain, swelling, warmth, tenderness at pulse-generator–pocket site, purulent drainage from generator pocket, drainage erosion of the pulse generator, and intraoperative evidence of pocket infection. Please see text for interpretation.

Device Explantation

All patients except 1 underwent hardware removal during the index hospitalization. The PPM was not removed in 1 patient because of advanced age and decompensated heart failure (Table 5, case 2). Forty-two patients (95%) had hardware removal at their initial presentation, whereas 1 patient had device explantation after failure of conservative management. Median duration from the date of admission to device removal was 4.5 days (IQR, 2-8 days).

Percutaneous explantation of transvenous leads was attempted in 36 patients, using manual traction (7 [19%]), locking stylet with laser sheath assistance (16 [44%]), or locking stylet without laser sheath assistance (13 [36%]), and was successful in 34 (94%) of these cases. Device leads were safely removed percutaneously in 15 patients who had greater than 10-mm vegetation attached to the intracardiac portion of the lead, without clinically important pulmonary embolism. Percutaneous lead extraction was complicated by pocket hematoma in 2 cases. Nine patients (16%) underwent surgical lead extraction by median sternotomy (2 after failure of percutaneous removal). Surgical lead extraction resulted in complications in 2 cases. One patient had subclavian vein laceration, whereas surgery resulted in ventriculotomy in another patient, requiring surgical repair during the procedure.

A replacement cardiac device was necessary in 26 (67%) of 39 patients who survived hospitalization (20 PPM, 6 ICD). Median time from removal of an infected device to placement of a new system was 9.5 days (IQR, 7-

TABLE 4. **Echocardiographic Findings in 44 Patients With Cardiac Device–Related Infective Endocarditis**[a]

Variable	No. (%)
Location of vegetation	
Electrode lead only	26 (59)
Cardiac valve leaflet only	6 (14)
Both (electrode lead and valve leaflet)	12 (27)
Valvular involvement	
Tricuspid valve	11 (25)
Pulmonary valve	1 (2)
Mitral valve	3 (7)
Aortic valve	5 (11)
Lead vegetation revealed	
TTE	3/38 (8)[b]
TEE	35/38 (92)[b]
Valve vegetation revealed	
TTE	1/18 (6)[b]
TEE	18/18 (100)[b]
Electrode lead thrombus	5 (11)
Myocardial abscess	1 (2)

[a] Median vegetation diameter was 11 mm (interquartile range, 8-20 mm); 3 patients (7%) had transthoracic echocardiography (TTE) alone, 13 (29%) had transesophageal echocardiography (TEE) alone, whereas 28 (64%) had both TTE and TEE.

[b] Data were missing for some patients.

TABLE 5. **Causes of Deaths in Patients With Cardiac Device–Related Infective Endocarditis**[a]

Case No./ age (y)/ sex	Device	Comorbid conditions	Microorganism	Vegetation	Hardware removal	Comments
1/65/M	PPM	Hemodialysis, prosthetic AV, splenectomy, CHF	CoNS Lead	Lead	Complete (percutaneous)	Patient died of nosocomial pneumonia with *Pseudomonas aeruginosa*
2/79/M	PPM	CHF	CoNS	Lead, AV, TV	Not removed because of high operative risk	Patient died of sepsis and renal failure
3/49/F	PPM	Heart TX for cardiac amyloidosis, BMT	*Aspergillus fumigatus*	Lead	Complete (percutaneous)	Fungal endocarditis complicated by metastatic abscesses in liver, spleen, brain, lung, kidneys, and thyroid gland
4/53/M	ICD	Anticoagulation for atrial fibrillation, CHF	MSSA	Lead, TV	Complete (percutaneous)	Patient died of acute renal failure and cardiac arrhythmia
5/73/M	PPM	DM, CHF, COPD, polymyalgia rheumatica (patient receiving long-term steroids)	MSSA	Lead	Complete (after failure of conservative treatment)	Patient died of severe sepsis and renal failure
6/56/M	PPM	Liver TX for sclerosing cholangitis or cirrhosis, Hodgkin lymphoma, TV ring annuloplasty, splenectomy, CHF	MRSA	Lead	Complete (percutaneous)	Patient died of MRSA sepsis and small bowel perforation

[a] AV = aortic valve; BMT = bone marrow transplant; BSI = bloodstream infection, CHF = chronic heart failure; CoNS = coagulase-negative staphylococci; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; ICD = implantable cardioverter-defibrillator; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *S aureus*; PPM = permanent pacemaker; TV = tricuspid valve; TX = transplant.

14 days). A temporary pacing lead was placed at the time of extraction in 14 patients (36%) who were device dependent, typically on the opposite side of the infected system. A new pulse generator was placed in the pectoral area (contralateral to an infected pocket) in 24 cases (55%), and 2 patients (5%) had abdominal generator placement. Lead placement was transvenous in 25 cases (57%), and epicardial patches were placed in 1 patient.

Antimicrobial Treatment

All patients received intravenous antibiotics during hospitalization. Eighteen patients (41%) received a combination of oral and intravenous antibiotics. β-Lactam agents (22 patients [50%]) and vancomycin (15 [34%]) were the most commonly used antibiotics. Median duration of intravenous antibiotics after device removal was 28 days (IQR, 14-36 days), and median duration of combined intravenous and oral antimicrobial treatment (after explantation) was 28 days (IQR, 19-42 days). Complications of antibiotic treatment included nephrotoxicity (5 [11%]), diarrhea (5 [11%]), hepatotoxicity (1 [2%]), and *Clostridium difficile* infection (1 [2%]).

Outcome

The median duration of hospitalization was 18 days (IQR, 13-23 days). Five patients (11%) died during index hospitalization for CDIE. Clinical presentation, management, and hospital course of these 5 patients are summarized in Table 5 (cases 1-5). Four of the deaths were directly attributable to device infection; a fifth patient died of nosocomial pneumonia with *Pseudomonas aeruginosa*. Of the remaining 39 patients, follow-up data were available in 28 cases (72%). Median duration from initial presentation with CDIE to last follow-up appointment was 183 days (IQR, 36-628 days). Twenty-seven (96%) of these 28 patients were infection free at the last follow-up visit. One patient had reinfection of the cardiac device (Table 5, case 6). This patient initially presented with pacemaker lead endocarditis and was managed by complete hardware removal followed by 6 weeks of parenteral antibiotics. A new PPM was placed before hospital discharge. Three months later, he had relapse of *S aureus* bacteremia secondary to a hemodialysis catheter infection with subsequent seeding of the new PPM. He died of sepsis and renal failure during the second hospitalization.

DISCUSSION

Our study is one of the larger reported series of CDIE; 44 (23%) of 189 patients with cardiac device infection had CDIE. This is much higher than that (≈10%) reported in the literature.[10,11,28] This incongruity likely results, in part, from the lack of a uniform case definition of CDIE previously and higher use of echocardiography in our study than in earlier reports. In one series,[28] presence of lead or valvular vegetation on TTE or TEE was the only criterion for a

diagnosis of CDIE. Others[11-13,15,29-31] had more complex criteria, using "modified versions" of the Duke criteria.[20,21] Most series have included positive lead-tip cultures as a major criterion for definite CDIE. In a recent study by Massoure et al,[15] 6 patients with positive lead cultures but no vegetations on echocardiography were classified as having definite endocarditis. The use of positive lead cultures as a criterion, however, can be misleading. Currently, most transvenous leads are percutaneously extracted via a generator pocket where a sterile lead is dragged (with or without a sheath) through an infected field. If the lead tip is contaminated and in turn yields a positive culture, a pocket infection could easily be erroneously classified as CDIE and could affect a decision on duration of antimicrobial therapy.

We assessed the utility of positive lead tip cultures as a criterion in establishing a diagnosis of CDIE among patients with PPMs or ICDs who were admitted to our institution with cardiac device infection. During the study period, 189 patients were admitted to MCR with device infection, 44 of whom were classified as having CDIE on the basis of our study definition. Among the 189 cases of device infection, 65 patients (34%) had positive lead tip cultures (Figure). Thirty-one (48%) had negative blood cultures and clinical evidence of pocket infection; 27 (87%) had a similar microorganism isolated from cultures of a generator pocket and a lead tip.

In these cases, the possibility of intraoperative contamination of the lead tip cannot be excluded. Ten (32%) of the 31 patients had lead or valve vegetations on echocardiography, were classified as having CDIE, and were treated with 4 weeks of antibiotics after device removal. The remaining 21 patients (68%) were treated as having pocket infections: 10 to 14 days of antimicrobial treatment after device removal. There were no cases of infection relapse or treatment failure. Classifying cases with only positive lead-tip cultures (negative blood cultures and no evidence of vegetations by echocardiography) as CDIE would unnecessarily prolong treatment. Positive lead-tip cultures can be used as a major criterion for CDIE only when there is no microbiological or clinical evidence of pocket infection, when leads are removed by a remote incision from the infected pulse-generator pocket (eg, extraction via a femoral vein),[32,33] or when leads are surgically removed by cardiotomy. In addition, lead cultures can be biologically negative in cases of CDIE because of antimicrobial administration before device removal or because biofilm is present, which could affect culture sensitivity in cases of device infection.[13]

In addition to the lack of a uniform case definition of CDIE, many of the previously published studies of CDIE made limited use of echocardiography. In the series reported by Arber et al,[11] only 21% of patients (99/468) underwent echocardiography. Moreover, only 2 patients underwent TEE. In contrast, all patients in our series underwent echocardiography, and most (28 [64%]) underwent both TTE and TEE (Table 4). Of the 28 cases, 14 (50%) had valvular vegetations, and 10 (36%) had lead vegetations seen on TEE alone. Tricuspid valve vegetations were detected by TTE in only 1 (4%) of 28 cases. This further demonstrates the extremely low sensitivity of TTE[12,13,15,16,34] for detection of device-related valvular and lead vegetations. Therefore, TEE should be performed in all cases of suspected CDIE, ie, in patients with positive blood cultures or systemic signs and symptoms. In addition to pointing toward accurate diagnosis of CDIE, TEE can assist in defining the most appropriate extraction technique by identifying patients with myocardial abscess or extremely large (>5 cm) lead vegetations that will necessitate surgery rather than a percutaneous method of lead extraction.

Original[20] or modified Duke criteria[21] do not specifically address diagnosis of PPM- or ICD-related infective endocarditis. If we include echocardiographic findings of lead vegetations as a major criterion in the Duke criteria, 34 (77%) of our cases would be classified as "definite" CDIE and 10 cases (23%) would be categorized as "probable" CDIE. When positive cultures from pulse-generator–pocket tissue or swabs are included as a major criterion, 41 (93%) of our cases are classified as "definite" CDIE and 3 cases (7%) as "probable" CDIE. Therefore, we believe that presence of lead vegetations and clinical evidence of generator-pocket infection should be included in the modified Duke criteria when diagnosing and classifying CDIE.

Staphylococci, the most common pathogens isolated in our investigation, accounted for 36 (82%) of organisms cultured (Table 3). This is consistent with previously published series of pacemaker endocarditis[11,15,16,29] and is likely secondary to the pathogens' ability to adhere to device surfaces and survive. Biofilm production has an important role in the pathogenesis of device infection.[35] Eighteen (41%) of isolated staphylococci infections were coagulase-negative staphylococci; 15 (34%) were methicillin-sensitive *S aureus,* and 3 (7%) were methicillin-resistant *S aureus*. Therefore, empiric medical treatment of suspected CDIE should include coverage for staphylococci, including methicillin-resistant strains.

There is abundant evidence that the optimal therapy for CDIE combines complete device extraction and a prolonged course of parenteral antibiotics. Reported mortality rates of CDIE range from 31% to 66% in cases managed conservatively (antibiotics alone) in contrast to 13% to 21% among patients who undergo complete device removal followed by prolonged treatment with systemic antibiotics.[12,13] In a recent series[15] of patients with pacemaker endocarditis, leaving the device intact was associated with

increased mortality ($P<.02$). Retaining the device is associated with a high risk of relapsing or persistent infection.[23,31,36] The mortality rate in our case series was 14%. This relatively low mortality rate is likely secondary to complete and early device removal and use of percutaneous extraction techniques instead of thoracotomy in most cases.[37] Forty-two patients (95%) had complete device explantation at initial presentation (median 4.5 days from admission to device removal; IQR, 2-8 days). One patient had device explantation after conservative treatment failed. A pacemaker was not removed in 1 remaining case because of an estimated high operative risk; the patient died of sepsis and renal failure (Table 5, case 2). Five other patients died despite complete device removal (Table 5); 4 were severely immunocompromised (2 had received allografts; 1 received prolonged corticosteroid therapy, and 1 had had a splenectomy). No cases of relapsing infection were identified at the last follow-up visit.

Percutaneous techniques are currently the method of choice for transvenous lead extraction. Some experts express concern that, with larger vegetations (>10 mm), percutaneous extraction can cause embolization of a lead vegetation into the pulmonary vasculature.[13] This concern is chiefly theoretical, and the published literature does not support this opinion.[16,23,37] In our study, percutaneous lead extraction was uncomplicated in 15 patients who had large (>10 mm in diameter) lead vegetations. Although routine screening for subclinical pulmonary embolism by computed tomography or ventilation-perfusion scanning was not performed, no patient developed clinical signs or symptoms of pulmonary embolism. This observation is consistent with data from a recently published series.[37] Some authors have postulated that emboli from lead vegetations are of minimal consequence because they are friable, as compared with the solid form of venous thrombi.[38-40] Leads were removed by median sternotomy in 5 of our patients with vegetations greater than 2.5 cm. Four of the 5 patients were considered at high risk for symptoms of pulmonary embolism, and the remaining patient had constrictive pericarditis that necessitated surgical intervention. Surgery was complicated by a ventricular tear in 1 patient and tricuspid valve damage in another; both patients had repairs during surgery for device removal and did well.

After complete hardware extraction and control of infection, the need for a replacement device must be carefully assessed. One-third of patients in our series did not require device reimplantation. This is consistent with a recently published series of endocarditis associated with implanted pacemakers.[15] Timing of reimplantation is subject to debate. Whereas some authors recommend delaying reimplantation for as long as 6 weeks in cases of CDIE,[41] others recommend that a new device be inserted when patients are no longer bacteremic.[10] In our series, the median time from removal of an infected device to placement of a new system was 9.5 days (IQR, 7-14 days) without infection relapse in any patient. At our institution, once a generator pocket is debrided, it is surgically closed, and a drain is placed. After drain removal, blood cultures are obtained; if they remain negative for at least 72 hours, then we proceed with reimplantation of a new device on the contralateral side.

Duration of antibiotic treatment after removal of an infected device has varied in different studies. Some authors have recommended at least 6 weeks of parenteral antibiotics after removal of an infected device.[41,42] However, considering that most cases of CDIE are limited to infection of the right side of the heart, a shorter course of 4 weeks could be adequate once a device has been removed.[30,43-45] In our series, the median duration of antibiotic therapy after removal of an infected device was 28 days (IQR, 19-42 days) without an increased incidence of relapse. Some have advocated an even shorter course of 2 weeks or less in cases of isolated lead infection. In a series of pacemaker and defibrillator lead infection by Dumont et al,[30] 8 patients who had vegetations strictly localized to leads without affecting cardiac valves recovered with fewer than 14 days of antibiotic therapy after explantation. However, many clinicians would treat patients with lead vegetations for at least 4 weeks of antibiotics even with echocardiographically unaffected cardiac valves. More data are needed to clarify these issues.

Our study has several limitations, the first of which is its retrospective design. Second, MCR is a tertiary referral center with potential referral bias. Third, both TTE and TEE were performed in only 28 patients (64%), which limits our ability to estimate the sensitivity of both methods of echocardiography accurately in detection of lead vegetations. In all instances of percutaneous extraction, device leads were pulled through the generator pocket, limiting our ability to assess the importance of positive lead cultures in the diagnosis of CDIE in cases of generator-pocket infection. Finally, follow-up data after hospital discharge were unavailable for 11 patients (25%), and this limits our assessment of long-term outcome.

CONCLUSION

Modifications in the Duke criteria are needed to increase their utility in the diagnosis of CDIE. Prompt and complete hardware removal followed by 4 weeks of antimicrobial treatment reduced mortality in patients with CDIE. Percutaneous removal of device components is successful and safe in nearly all patients, even when lead vegetation diameters are greater than 10 mm.

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