JOURNAL of the
SAUDI HEART
ASSOCIATION

Official Journal of the Saudi Heart Association
PREVALENCE AND OUTCOME OF BACTERIAL ENDOCARDITIS IN PATIENTS WITH IMPLANTABLE CARDIAC DEVICE INFECTIONS

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Background: Cardiac device infection (CDI) is a devastating complication of permanent pacemakers (PPM) or implantable cardioverter-defibrillators (ICD). The incidence and outcome of endocarditis among patients with CDI is not well defined.

The aim of this study was to report our experience in the prevalence, clinical presentations, and management of bacterial endocarditis (BE) among patients with CDI in a tertiary care cardiac center over a 25-year period.

Methods: A total of 2630 cardiac devices implanted in a cohort of 2367 patients over 25 years were studied. Of these, 117 (4.4%) patients presented with CDI. Clinical, bacteriologic and both transesophageal echocardiographic (TEE) and transesophageal echocardiographic (TEE) assessments were done.

Results: Of the 117 patients with CDI (90 males, age range 18-82 yrs, mean = 63 ± 6 yrs), 87 (74%) had redo procedures (battery replacement in 50, repositioning of leads in 12, device extrusion in 15 or evacuation of significant haematoma in 10 patients). Of these 87 patients, 65 had re-implants on the same day of explanation. In 30 patients (26%) no apparent cause of PI was identified. Of the 117 patients with CDI, 30 patients (26% of CDI and 1.1% of total procedures) had device-related BE with vegetations having appeared in all patients by TEE (15 DDD, 9 VVI, 3 CRT & 3 ICD). The clinical presentations were prolonged fever in 25 patients (83%), significant pulmonary hypertension with thrombo-embolism in 3 patients (10%), severe sepsis and multi-organ failure in 2 patients (6%). Twenty-eight patients (93%) had positive blood cultures (S. aureus in 23 [77%] and enterococci in 5). There were only 2 patients with negative blood cultures. Device lead vegetations were evident in 20 patients (>10 mm diameter in 13 patients). Ten patients presented with only right heart valve vegetations. Of the 30 BE patients, 28 (93%) had PI while 2 patients had no apparent cause but frequent intravenous injections (one drug addict and one on regular haemodialysis). Of the 20 patients with lead endocarditis, 15 had their leads removed surgically with re-implantation of either epicardial (6 patients) or endocardial leads (9 patients). Fifteen patients had only medical treatment with proper antibiotics (5 patients with lead BE and all 10 patients with valvular BE). Four patients (13%) died; all had their devices implanted on same day of explanation.

Conclusion: Cardiac device redo procedures are major risk factors for CDI, especially with re-implantation on the same day. Device-related BE carries a serious morbidity and mortality, yet surgical removal of the whole system is the management of choice. Blood stream bacteremia is a potential risk factor in patients with cardiac devices and warrants prophylaxis against BE.

Key words: bacterial endocarditis - pacemakers - echocardiography

Introduction

WITH AN INCREASING NUMBER of indications for use of permanent pacemakers (PPM) and implantable cardioverter-defibrillators (ICD), there have been more complications of these interventions. Infection secondary to cardiac device implantation is a major factor in morbidity and mortality.¹ Management of CDI is a difficult challenge for both cardiologists and infectious disease specialists. The incidence of infection following implantation has been variably assessed as ranging from 0.13%² to 19.9%.³ Early diagnosis and accurate localization of infection along the lead or on the endocardium are two major issues. Local inflammation at the site of the pulse generator pocket clearly indicates infection. On the other hand, sepsis involving only the lead raises major diagnostic problems that may result in delayed...
treatment and poor outcome. The time interval between the last intervention and the onset of infection distinguished early (up to two weeks), intermediate (two weeks to six months), and late onset infections (more than six months).

The risk of developing bacterial endocarditis (BE) in the setting of cardiac device infection (CDI) is inadequately defined. This uncertainty complicates patient management. Clinicians caring for patients with permanent pacemakers or implantable cardioverter-defibrillators who develop CDI often have difficulty in estimating the likelihood of device BE, leading to diagnostic and therapeutic delays.

Thus, the objective of the present investigation was to determine the incidence of BE in patients presenting with CDI. To achieve this objective, we retrospectively evaluated 2367 consecutive patients with cardiac devices over 25 years.

Patient and Methods

Over the past 25 years, starting from 1982, 2630 implants (2177 permanent pacemakers, 221 cardiac resynchronization therapy and 232 implantable cardioverter defibrillators) were performed in 2367 patients at the Critical Care Medicine Department of Cairo University hospitals.

Out of these, we retrospectively studied 117 (5%) patients who presented with cardiac device infection (CDI). They were subjected to clinical, bacteriologic and echocardiographic assessment (both transthoracic (TTE) and transoesophageal (TEE)). Because permanent pacemakers and implantable cardioverter defibrillators are structurally similar, patients were included in the present study if either device was present at the time of their CDI.

We mean by CDI any patient with permanent pacemaker-related infections including pocket infection and/or leads bacterial endocarditis.

Clinical assessment: Evidence of pocket infection was defined as erythema, warmth, fluctuance, wound dehiscence, erosion, tenderness or purulent discharge with or without fever at the generator site.

It was microbiologically confirmed if blood and/or wound cultures from the generator pocket were positives.

Endocarditis was clinically confirmed when valvular or lead vegetations were detected by echocardiography, or if the Duke criteria for infective endocarditis were met. 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.

Echocardiographic examination TTE was conducted to assess both left and right ventricular dimensions and functions, signs of pulmonary hypertension and presence of valvular or lead vegetations. In the latter case, diagnosis was confirmed by TEE to exactly measure location, structure and size of vegetations. To reduce potential bias created by sequential readings, all transoesophageal echocardiograms were later reinterpreted in a blinded manner by one of the investigators.

Results

Over the last 5 years, 710 implants were performed in 682 patients. The total number of implants over the 25-year period of the study was 2630 in 2367 patients. The group of patients studied comprised 117 patients whose demographic data are depicted in Table 1. Indications for device implantation were permanent pacing in 92 (63 dual, and 29 single chamber), 10 cardiac resynchronization therapy (CRT) and 15 implantable cardioverter defibrillators (ICD). Thirty patients were confidently diagnosed with BE, constituting 26% of all CDI patients and 1.1% of total implantation procedures.

Clinical Presentation and Microbiology: There was considerable variation in time from device implantation to onset of infection in our survey. The median time from device implantation to infection was 415 days (range, 120-744 days). All patients had localized inflammatory signs at the pocket site (Figure 1). The clinical presentations were prolonged fever in 25 patients (83%), significant pulmonary hypertension with thrombo-embolism in 3 patients (10%), severe sepsis and multi-organ failure in 2 patients (6%).

Patients studied were divided into 2 groups for comparison. Group I were those with CDI, but no evidence of endocarditis by TEE. This group comprised 87 patients. The other group comprised those with CDI and evident BE by virtue of vegetations on TEE (group II, 30 patients) (Table 1).
### Table 1. Clinical Characteristics of study patients

<table>
<thead>
<tr>
<th></th>
<th>Group I CDI without BE (87 pts)</th>
<th>Group II BE patients (30 pts)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>mean 56 ± 1 (18 – 78 yrs)</td>
<td>mean 62 ± 1.5 (23 – 82 yrs)</td>
<td>NS</td>
</tr>
<tr>
<td>Male sex</td>
<td>67</td>
<td>23</td>
<td>NS</td>
</tr>
<tr>
<td>Associated conditions:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Diabetes mellitus</td>
<td>34 (39%)</td>
<td>12 (40%)</td>
<td>NS</td>
</tr>
<tr>
<td>*Haemodialysis dependency</td>
<td>6 (7%)</td>
<td>2 (7%)</td>
<td>NS</td>
</tr>
<tr>
<td>*Systemic hypertension</td>
<td>45 (52%)</td>
<td>15 (50%)</td>
<td>NS</td>
</tr>
<tr>
<td>*Dilated cardiomyopathy</td>
<td>12 (14%)</td>
<td>2 (7%)</td>
<td>NS</td>
</tr>
<tr>
<td>*Ischemic H.D</td>
<td>35 (40%)</td>
<td>12 (40%)</td>
<td>NS</td>
</tr>
<tr>
<td>*Congenital H.D</td>
<td>14 (16%)</td>
<td>2 (7%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

CIDI cardiac device infection  PPM permanent pacemaker  BE bacterial endocarditis  CRT cardiac resynchronization therapy  ICD implantable cardioverter defibrillator  NS not significant

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**Figure 1.** Extruded permanent pacemaker with pocket infection.

**Figure 2.** Vegetation on pacemaker lead (15 x 11 mm dimensions) at tricuspid valve level as seen by transthoracic echocardiography (PML: pacemaker lead).

**Figure 3.** Vegetation (veg) on pacemaker lead (20 x 17 mm dimensions) at right atrial (RA) cavity level as seen by transesophageal echocardiography. AO = aorta.

### Management & Outcome

In group II patients, with BE, out of the 30 patients, 28 (93%) had positive blood cultures (S. aureus in 23 and enterococci in 5). There were only 2 patients with negative blood cultures.

Antimicrobial treatment: All patients received antimicrobials after removal or debridement of infected device system. All patients received at least 2 weeks of antibiotics after removal of an infected device. Median duration of antibiotic treatment was significantly longer in patients with BE. Fifteen patients had only medical treatment with proper antibiotics (5 patients with lead BE and all 10 patients with valvular BE). Device lead vegetations were evident in 20 patients (>10 mm diameter in 13 patients), (Figures 2, 3). Ten patients presented with only right heart valve vegetations. Out of the 30 BE patients, 28 (93%) had PI while 2 patients had no apparent cause but frequent intravenous injections (one drug addict and one on regular haemodialysis).

Of the 20 patients with lead endocarditis 15 had their leads removed either endocardially (5 patients) or surgically (10 patients with large vegetations) via median sternotomy and cardiomyotomy with re-implantation of either an endocardial or epicardial leads respectively (Figures 4, 5). Four patients (13%) died (2 with septic shock, one with multi-organ failure, and one with progressive heart failure) and all had their generators re-implanted on same day of explantation.
Comparison between BE and CDI without BE

We compared both groups as regards:
1. Prevalence of pocket infection.
2. Redo procedures either for explantation, re-implantation or evacuation of significant haematoma.
3. Whether re-implantation was on same day of explanting the infected system.
4. Whether the same old potentially infected lead was left in place at time of explanting infected devices (Table 2).

Table 2. Comparison between groups in incidence of device infection complications

<table>
<thead>
<tr>
<th></th>
<th>Group I (87 pts)</th>
<th>Group II (30 pts)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Pocket infection</td>
<td>86 (99%)</td>
<td>28 (93%)</td>
<td>NS</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Related to CDI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Haematoma</td>
<td>8 (9%)</td>
<td>2 (6%)</td>
<td>NS</td>
</tr>
<tr>
<td>*Total Redo procedures</td>
<td>59 (68%)</td>
<td>28 (93%)</td>
<td>NS</td>
</tr>
<tr>
<td>Same day</td>
<td>44 (50%)</td>
<td>27 (90%)</td>
<td>0.05</td>
</tr>
<tr>
<td>*Mortality</td>
<td>NONE</td>
<td>4 (13%)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

There was no significant difference between both groups regarding incidence of haematoma, device extrusion or total redo procedures (9%, 40%, and 68% in group I vs. 6%, 47%, and 93% in group II, respectively). However, more patients with BE tended to be exposed to more redo procedures than patients without BE. On the other hand, patients in group II (BE patients) had a significantly higher redo procedures in the same day than group I patients (90% vs. 50%, P 0.05, respectively). Mortality was significantly higher in BE group (13%) than the other group (p= 0.01).

Discussion

We previously reported our experience over the 20 years since 1982 with follow up of pacemakers and showed that pocket infection and device extrusion represented the second commonest cause (20.5%) of device replacement only after battery end of life (44.4%). We showed that the most important predisposition for pocket infection was wound reopening for various etiologies as repositioning of leads or evacuation of haematomas. In the present study, we are reporting the results of all previous records of the critical care department of Cairo University over 25 years. It is obvious that the total number of patients and implants over the last 5 years has increased (682 patients and 710 implants, respectively) compared to the same period of 5-year follow-up studies.3,9,10 The total number of implants (2630) was analyzed in the present study (Table 3). The increased percentage of PI among the whole cohort of patients can be explained by the increased referrals of an increasing population to our center from many centers on one hand and to the increasing awareness and diagnostic facilities of device complications on the other hand.

The clinical and microbiologic analysis of BE
patients showed significant variation, ranging from non-specific symptoms and signs (low grade fever, malaise and swelling) to more specific and definitive criteria of diagnosis (positive blood cultures and documented vegetations by TEE). S. aureus was the most common organism isolated (77%), which is consistent with the results of Chamis et al.11 who found that S. aureus bacteraemia had CDI accompanied by 75% endocarditis in patients with implanted devices when found early (first 1 year after device placement) and in 71% of late (more than 1 year). However, they concluded that neither physical examination nor echocardiography could exclude the possibility of CDI. Sohail et al.12 emphasized the same conclusions of misleading cardiac symptoms and signs of infection in diagnosing CDI in a large cohort of 189 CDI patients.

Table 3 Prevalence of pocket infection in various studies conducted in the Critical Care Department

<table>
<thead>
<tr>
<th>Studies conducted in same center</th>
<th>Pts No.</th>
<th>Implants No.</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taieb et al. (from 1992-1993) (8)</td>
<td>578</td>
<td>648</td>
<td>3.7%</td>
</tr>
<tr>
<td>Moharam et al. (from 1994-1998) (9)</td>
<td>525</td>
<td>639</td>
<td>3.9%</td>
</tr>
<tr>
<td>Andraos et al. (from 1998-2002) (10)</td>
<td>554</td>
<td>625</td>
<td>3.6%</td>
</tr>
<tr>
<td>Present study (from 1982 till date)</td>
<td>2630</td>
<td>2367</td>
<td>4.4%</td>
</tr>
</tbody>
</table>

Use of the temporary pacing wires has been identified as a risk factor for subsequent CDI in 2 recent studies.23, 24 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.25,11 Based on the above findings, we recommend complete hardware removal to achieve CDI cure; this mirrors the recommendations of the American Heart Association.25

Percutaneous Versus Surgical Lead Extraction

Extraction of cardiac device leads is not without risk.26 Despite advances in techniques for percutaneous lead extraction, there is still considerable morbidity and mortality associated with this procedure. In our study, 5 patients had their devices and lead percutaneously extracted. 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.27,28 No patient had a clinically significant pulmonary embolism in our series despite the presence of pulmonary hypertension in two patients, indicating possible recurrent subclinical embolizations. Others have reported similar experiences.

Incidence of CDI and BE

The estimated rate of cardiac device infection after permanent endocardial pacemaker (PPM) or implantable cardioverter-defibrillator implantation has varied from 0.13% to 19.9% in old reports.32,33 In our old reports CDI incidence rates varied between 3.6-3.9 %.4,10 In the present study the incidence of CDI and bacterial endocarditis was 4.4 %, and 1.1%, respectively. Although these incidences are higher than those reported in our previous investigations,39 the increased accuracy of diagnosing device-related BE using TEE with improved imaging techniques and resolution can at least partially explain this.

Study Limitations

Our investigation has several limitations. First, retrospective studies have inherent limitations, such as potential selection and recall biases. Second, the EP service in the critical care department 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. Despite these limitations, data presented herein provide critical information to clinicians who manage CDI.

Conclusions

A CDI is an important and serious complication of cardiac devices use. Yet BE is a more devastating event that better be avoided. 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 can conclude from the present study that:

* Removal of the whole system (Generator and leads) is the management of choice either percutaneously (for vegetations less than 10 mm diameter) or by surgical open cardiomyotomy for larger ones with new epicardial permanent pacemaker implantation.
Implantable Cardiac Device Infections

* Blood stream bacteraemia is a potential risk factor in patients with cardiac devices and warrants prophylaxis against BE by aggressive antimicrobial agents.

* At least a 2-week lapse period between explanting infected systems and re-implantation of endocardial permanent pacemaker is highly recommended in treatment of pocket infection patients.

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