Bacterial Contamination During Pacemaker Implantation Is Common and Does Not Always Result in Infection

Masato Okada, MD; Kazunori Kashiwase, MD, PhD; Akio Hirata, MD, PhD; Takayoshi Nemoto, MD; Koshi Matsuo, MD; Ayaka Murakami, BSc; Yasunori Ueda, MD, PhD

Background: Bacterial cultures of cardiovascular implantable electronic devices removed from patients without clinical infection are often positive, and the cultured bacteria are different from those at the time of clinical infection. This discrepancy has not been adequately explained. We hypothesized that the cause is bacterial contamination at operation and compared the results of bacterial cultures between patients with de novo pacemaker implantation and those with pacemaker replacement.

Methods and Results: We prospectively enrolled consecutive 100 patients who underwent cardiac pacemaker implantation (49 de novo implantations, 51 replacements). We took swab cultures from inside the generator pocket (1) immediately after the creation of new pocket or removal of old generator, (2) after connection of leads to new generator, and (3) after pocket lavage. Swab cultures were positive in 272 (45%) of 600 samples. The majority of the cultured bacteria were Propionibacterium species. No statistical difference was detected between de novo implantations and replacements in the positive ratio of swab cultures. The positive ratio was not correlated with the number of previous device replacements.

Conclusions: The positive ratio of swab cultures was not different between new implantations and replacements, suggesting that a positive culture merely indicates contamination of bacteria during operation rather than colonization.

Key Words: Bacterial colonization; Cardiovascular implantable electronic devices; Infection

Infection related to cardiovascular implantable electronic devices (CIED) is a serious complication with high mortality and morbidity, necessitating removal of the device and prolonged antibiotic therapy. However, using sonication fluid and conventional swabs from removed CIED, Rohacek et al demonstrated positive bacterial cultures in approximately 40% of patients and suggested that bacteria do not always cause clinical infection, some colonizing CIED without clinical signs of infection. The results of another report by Mason et al on asymptomatic colonization are consistent with that report. This discrepancy in the culture results has not been adequately explained.

We hypothesized that it might be the result of misinterpretation of positive bacterial cultures. In other words, positive cultures might be the result of contamination rather than the colonization. Because the previous 2 reports did not have a control group to differentiate contamination and colonization, we examined and compared the results of bacterial cultures between patients with de novo pacemaker implantation and those with pacemaker replacement. If colonization exists, the positive ratio of the cultures should be higher in patients with replacement than in those with de novo implantation.

Editorial Information

In both reports, bacterial cultures were examined in patients from whom the CIED was removed without signs of clinical infection, and the majority of cultured bacteria were Propionibacterium species represented by P. acnes. However, at the time of CIED infection, the majority of cultured bacteria are known to be coagulase-negative Staphylococcus (eg, S. epidermidis) or S. aureus. This discrepancy in the culture results has not been adequately explained.

Study Patients

We performed a prospective, observational, single-center cohort study in Osaka Police Hospital, Osaka, Japan. We prospectively enrolled 100 consecutive patients who underwent cardiac pacemaker implantation from August 2012 to May 2013: 49 patients underwent de novo implantation and 51 patients received a replacement. Because it is well known that a larger device presents a greater opportunity for infection, we included pace-
Procedures of Device Implantation

Implantation and replacement of devices were performed in the catheterization laboratory. The level of cleanliness of the catheterization laboratory was similar to that of the operating room, as it satisfied Class II conditions of the Healthcare Engineering Association of Japan HEAS-02-1998 and Class 8 conditions of ISO14644-1. The patients came to the catheterization laboratory after being shaved and swabbed with 4% chlorhexidine solution. We lavaged each patient’s skin twice with 0.5% chlorhexidine gluconate and 7.5% povidone-iodine solution using sterile cloths. Operators and assistants wore surgical gowns and double sterile gloves. Surgical drapes coated with povidone-iodine (3M™ Ioban™ 2 antimicrobial incise drapes, Minnesota Mining and Manufacturing Company, St. Paul, MN, USA) were used to reduce the risk of contamination from skin flora during the procedure. Antibiotic (1 g cefazolin) was routinely administered immediately before and at 6 h after operation.

Table. Characteristics of the Study Patients Undergoing De Novo Pacemaker Implantation or Device Replacement

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>De novo</th>
<th>Replacement</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>100</td>
<td>49</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>74±12</td>
<td>75±11</td>
<td>73±13</td>
<td>0.3</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>57 (57)</td>
<td>29 (59)</td>
<td>28 (55)</td>
<td>0.6</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.2±5.8</td>
<td>23.0±4.7</td>
<td>22.7±3.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Serum albumin, g/dl</td>
<td>4.0±0.5</td>
<td>3.9±0.6</td>
<td>4.1±0.4</td>
<td>0.009</td>
</tr>
<tr>
<td>Baseline disease, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>19 (19)</td>
<td>13 (27)</td>
<td>6 (12)</td>
<td>0.06</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>28 (28)</td>
<td>19 (39)</td>
<td>5 (18)</td>
<td>0.02</td>
</tr>
<tr>
<td>Prosthetic heart valve</td>
<td>7 (7)</td>
<td>6 (12)</td>
<td>1 (2)</td>
<td>0.05</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>32 (32)</td>
<td>19 (39)</td>
<td>13 (26)</td>
<td>0.1</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>5 (5)</td>
<td>4 (8)</td>
<td>1 (2)</td>
<td>0.1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>22 (22)</td>
<td>11 (22)</td>
<td>11 (22)</td>
<td>0.9</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>4 (4)</td>
<td>0 (0)</td>
<td>4 (8)</td>
<td>0.04</td>
</tr>
<tr>
<td>Malignancy</td>
<td>9 (9)</td>
<td>5 (10)</td>
<td>4 (8)</td>
<td>0.7</td>
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<tr>
<td>Echocardiographic parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Diastolic left ventricular diameter, mm</td>
<td>50±5</td>
<td>50±6</td>
<td>50±4</td>
<td>0.9</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>66±11</td>
<td>66±12</td>
<td>66±11</td>
<td>0.8</td>
</tr>
<tr>
<td>Medications, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>22 (22)</td>
<td>15 (31)</td>
<td>7 (14)</td>
<td>0.04</td>
</tr>
<tr>
<td>Oral anticoagulant</td>
<td>26 (26)</td>
<td>16 (33)</td>
<td>10 (20)</td>
<td>0.1</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>2 (2)</td>
<td>0 (0)</td>
<td>2 (4)</td>
<td>0.1</td>
</tr>
<tr>
<td>Reason for pacemaker implantation, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sick sinus syndrome</td>
<td>57 (57)</td>
<td>29 (62)</td>
<td>28 (57)</td>
<td>0.5</td>
</tr>
<tr>
<td>Atrioventricular block</td>
<td>39 (39)</td>
<td>18 (39)</td>
<td>21 (45)</td>
<td>0.5</td>
</tr>
<tr>
<td>Atrial fibrillation with bradycardia</td>
<td>4 (4)</td>
<td>2 (4)</td>
<td>2 (4)</td>
<td>0.9</td>
</tr>
<tr>
<td>History of prior pacemaker operations, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De novo implantation</td>
<td>49 (49)</td>
<td>49 (100)</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>1st replacement</td>
<td>24 (24)</td>
<td>0</td>
<td>24 (24)</td>
<td>–</td>
</tr>
<tr>
<td>2nd replacement</td>
<td>12 (12)</td>
<td>0</td>
<td>12 (12)</td>
<td>–</td>
</tr>
<tr>
<td>≥3rd replacement</td>
<td>15 (15)</td>
<td>0</td>
<td>15 (15)</td>
<td>–</td>
</tr>
<tr>
<td>Surgical procedure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operation time (min)</td>
<td>96±32</td>
<td>108±24</td>
<td>85±33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lead replacement</td>
<td>63</td>
<td>49 (100)</td>
<td>14 (28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Temporary pacing</td>
<td>5 (5)</td>
<td>4 (8)</td>
<td>1 (2)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Renal insufficiency is defined as estimated glomerular filtration rate <30 ml/min/1.73 m². Patients with diabetes mellitus are defined as those with hemoglobin A1c >6.5% or already taking diabetic medication.

makers only and excluded patients who received an implantable cardioverter defibrillator or cardiac resynchronization therapy device.

Patients’ clinical records were summarized with a standardized case report form to retrieve demographic, clinical, microbiological, and laboratory data. The following baseline characteristics were assessed: age, sex, nutritional state (body mass index and serum albumin concentration), heart disease (congestive heart failure and coronary artery disease), presence of prosthetic heart valves, immunosuppressive disease, renal insufficiency (estimated glomerular filtration rate <30 ml/min/1.73 m²), diabetes mellitus, liver cirrhosis, malignancy, corticosteroid use, echocardiographic parameters (diastolic left ventricular diameter and ejection fraction), intake of oral antplatelet agents and anticoagulants, the primary disease that required pacemaker therapy (sick sinus syndrome, atrioventricular block and atrial fibrillation bradycardia), and the number of previous device replacements.

The study protocol was approved by the Osaka Police Hospital ethical committee and all enrolled patients gave written informed consent.
### Clinical Outcome

After pacemaker implantation, patients were observed for approximately 1 week in hospital and checked for correct operation of the pacing and for any complications such as lead dislodgement, hematoma or signs of infection. After discharge, patients were routinely seen every 4 months to control device function and to check for signs of infection.

Infection was diagnosed as either local infection of the generator pocket (acute inflammation with redness, local warmth, pain, swelling and/or purulent drainage through incision or through skin erosion, but without systemic inflammatory symptoms) or pacemaker-associated infectious endocarditis, defined by the Duke criteria.16

### Statistical Analysis

Data are presented as mean±SD, number and percentage, and odds ratio with a 95% confidential interval. A Mantel-Haenszel test was used for univariate analysis to investigate the parametric risk factors of positive culture. Fisher’s exact test or Chi-square test was used for non-parametric factor evaluation. Multivariate analysis was performed using a conditional logistic regression model including all factors that were significantly associated with positive culture by univariate analysis. P<0.05 was regarded as statistically significant. Analysis was performed with SPSS version 16.0 J for Windows (SPSS inc, Chicago, IL, USA).

### Results

#### Patients’ Characteristics

Of the 100 enrolled patients, 49 received their first device and 51 underwent replacement of their pacemaker. The patients’ characteristics are presented in Table. There was no statistical difference in the patients’ age, sex or body mass index, but serum albumin level was lower in the patients with a first device than in those with a replacement. The patients undergoing de novo implantation had coronary artery disease, antiplatelet therapy, and prosthetic heart valves more frequently than those with a replacement device.

#### Culture Results and Bacterial Species

In no patients were bacteria detected by microscopic examina-
Culture Results and Sample Timing
At least 1 sample was positive at the 1st time point in 39 (39%) patients. The cultures were positive in 83 (42%), 90 (45%), and 94 (47%) samples at 1st, 2nd, and 3rd time points, respectively. The ratio of positive culture increased at the 3rd time point compared with the 1st time point (P=0.049); however, the difference was not statistically significant between the 1st and 2nd (P=0.30) or between the 2nd and 3rd time points (P=0.35) (Figure 5).

The positive ratio for any bacteria, *Propionibacterium* species or coagulase-negative *Staphylococci* (CNS), was not different between the samples from de novo implantation patients and those undergoing device replacement.

Figure 2. Comparison of cultured bacteria between (A) de novo implantation and (B) device replacement in 100 patients shows no difference between the 2 groups. The majority of cultured bacteria were *Propionibacterium* species in both groups. The positive ratio for *Propionibacterium* species or for coagulase-negative *Staphylococci* (CNS) was not different between the groups.

Figure 3. Comparison of cultured bacteria in 600 pacemaker pocket swab samples. The positive ratio for any bacteria (A), for *Propionibacterium* species (B) and for coagulase-negative *Staphylococci* (CNS) (C) was not different between the samples from de novo implantation patients and those undergoing device replacement.
Bacterial Culture of CIED

were consistent with 2 previous reports. Rohacek et al reported that approximately 40% of swab cultures were positive and that the majority of cultured bacteria were Propionibacterium species, represented by P. acnes. Mason et al reported that 21% of patients had positive cultures, and almost all of them

Clinical Outcomes
The study patients were followed up for 25±3 months. One patient developed a clinically apparent pacemaker infection at 397 days after pacemaker replacement. The 74-year-old male underwent pacemaker (DDD mode) implantation in May 2007 for sick sinus syndrome and atrioventricular block, and then pacemaker replacement in September 2012 because of insufficient battery charge. In October 2013 he presented with the chief complaint of erythema and swelling around the wound. Emergency removal of the pacemaker and leads was performed on the same day, and pacemaker re-implantation was performed after 1 month of antibiotic therapy. Although P. acnes had been cultured at the time of pacemaker replacement, coagulase-negative Staphylococci were cultured at the time of infection. Smear had revealed no bacteria at the time of pacemaker replacement, but there were Gram-positive cocci and white blood cells at the time of infection.

Discussion
In the present study we demonstrated that approximately one-half of the patients who received a first pacemaker or a replacement had positive results for bacterial culture swabs from the pacemaker pocket and that there was no significant difference in the positive ratio of the cultures between the 2 groups. Therefore, the positive cultures might be the result of contamination during operation rather than bacterial colonization.

Interpretation of Culture Results
Our results for the patients undergoing pacemaker replacement were consistent with 2 previous reports. Rohacek et al reported that approximately 40% of swab cultures were positive and that the majority of cultured bacteria were Propionibacterium species, represented by P. acnes. Mason et al reported that 21% of patients had positive cultures, and almost all of them
were skin flora.\textsuperscript{9} However, we demonstrated, for the first time, that the positive ratio of cultures was not different between patients with de novo pacemaker implantation and those with a replacement and that the majority of cultured bacteria were \textit{Propionibacterium} species normally present on human skin, and in sebaceous glands, and hair follicles. Therefore, these results could be significantly influenced by contamination rather than colonization, and the previous reports might have overestimated the bacterial colonization. Even if colonization exists, it is likely to be much less frequent than previously reported.

**Contamination, Colonization and Infection**

We know from studies of surgical site infection that the essential difference between contamination and colonization is the concentration of organisms in the wound.\textsuperscript{17,18} An infected wound contains a larger number of microorganisms than a contaminated wound. Although approximately one-half of the patients in the present study had positive culture results, there was only 1 late case of CIED infection, related to the fact that swab culture is a qualitative evaluation and its results do not reflect the concentration of organisms in the pacemaker pocket.

In our case of CIED infection, although \textit{P. acnes} had been cultured at the time of pacemaker replacement, coagulase-negative \textit{Staphylococci} was cultured at the time of infection, a result that is consistent with the previous report by Mason et al.,\textsuperscript{9} in which no patients with asymptomatic “colonization” developed clinical infection during the follow-up period. They concluded that a significant proportion of patients had asymptomatic “colonization”, although it was not a marker of future pocket infection. We should rephrase that a significant proportion of patients had contamination of bacteria during operation, but it was not a marker of future pocket infection.

In differentiating contamination, colonization, and infection, we should consider the following questions: (1) Can the cultured bacteria infect the target organ? (2) Does the patient have clinical symptoms of infection? and (3) Were the cultured bacteria also detected in the smear?\textsuperscript{\textsuperscript{19}} Because approximately 70\% of CIED infections have been reported as caused by coagulase-negative \textit{Staphylococcus} (eg, \textit{S. epidermidis} and \textit{S. aureus}), we should reconsider whether cultured bacteria could truly cause clinical infection when other bacteria are detected.\textsuperscript{1-7,20-22}

**Effect of Lavage Procedure**

The rate of positive culture in the present study was not different between before and after lavage of the pacemaker pocket with saline solution. However, in general wound management, irrigation with warm sterile saline is used routinely and believed to be effective in decreasing the bacterial load. Proper wound
cleansing and debridement can prevent bacterial colonization proceeding to clinical infection. The results of the swab cultures in the present study did not reflect the concentration of organisms in the pacemaker pocket, so the effect of lavage could not be evaluated correctly and remains inconclusive.

Contamination of the Surgical Field
The present study demonstrated a rather high incidence of contamination during operation and the frequency of clinical infection from contamination was 0.5% (1/55). We should realize that “uninfected CIED is sterile” might be a myth. Although contamination during operation can occur more frequently than we suppose, the Propionibacterium species mainly cultured at the time of pacemaker implantation would not cause clinically apparent pacemaker infection during follow-up.

Study Limitations
There are some important limitations in this study. Because the frequency of CIED infection is less than 1%, the number of enrolled patients was too small to evaluate clinical infection. Because it is not uncommon that the clinical presentation of CIED infection occurs >12 months after pacemaker implantation, the follow-up interval of the present study was inadequate for evaluating clinical infection. Environmental factors at the study institution might have influenced the frequency of contamination. There were some differences between the groups in the patients’ backgrounds, probably related to the small size of the study population. Coagulase-positive Staphylococci (ie, S. aureus), which are the main bacteria causing CIED infections, were not detected in any swab culture. However, the results of swab cultures are not quantitative and do not reflect the concentration of organisms in the pacemaker pocket.

Conclusions
Nearly half of the patients who underwent de novo implantation or a replacement had positive results for bacterial swab cultures from the pacemaker pocket. However, the positive ratio of the swab cultures was not different between the 2 groups of patients, suggesting that the positive cultures may be contaminated during operation rather than bacterial colonization.

Conflict of Interest

Funding Sources
None.

Financial Support
None.

Disclosures

References