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

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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 devises; 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.1–7 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.8 The results of another report by Mason et al on asymptomatic colonization9 are consistent with that report.

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.10–15 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 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.

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 cefazoline) 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

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

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.

The study protocol was approved by the Osaka Police Hospital ethical committee and all enrolled patients gave written informed consent.
Under continuous ECG monitoring, we injected local anesthetic (1% xylocaine), made a skin incision in the upper chest, and created a subcutaneous pocket using an electrosurgical knife. We inserted a sheath into an axillary vein and advanced a pacer lead wire through it to the heart. The lead was firmly attached to the heart muscle with a screw device. After checking the pacing and sensing thresholds, we connected the lead wire to the pulse generator, and lavaged the pocket with saline solution. After lavage, we placed the lead and device into the pocket and sutured the subcutaneous tissue and cutis vera.

In the case of pacemaker replacement, after opening the pocket, we removed the old device and checked pacing and sensing thresholds of the leads. If the threshold was inadequate, we implanted a new lead. After connecting the lead to a new generator, we lavaged the pocket with saline solution, placed the lead and device in the pocket, and sutured the subcutaneous tissue and dermis just below dermal-epidermal junction by using polydioxanone filament. We finally applied skin adhesives (DERMABOND HV, ETHICON, USA) to make a microbial barrier and wound closure integrity.

Swab Culture

Cotton-tipped swabs (BD BBL™ CulturesSwab™ EZ II, Becton, Dickinson & Co, Franklin Lakes, NJ, USA) were used to obtain 2 swab cultures from inside the generator pocket at 3 time points during the procedure, thus 6 samples from each patient. The 1st time point was immediately after the creation of a new generator, we lavaged the pocket with saline solution. After lavage, we placed the lead and device into the pocket and sutured the subcutaneous tissue and cutis vera.

In the case of pacemaker replacement, after opening the pocket, we removed the old device and checked pacing and sensing thresholds of the leads. If the threshold was inadequate, we implanted a new lead. After connecting the lead to a new generator, we lavaged the pocket with saline solution, placed the lead and device in the pocket, and sutured the subcutaneous tissue and dermis just below dermal-epidermal junction by using polydioxanone filament. We finally applied skin adhesives (DERMABOND HV, ETHICON, USA) to make a microbial barrier and wound closure integrity.

Results

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-
tion of the Gram-stained smear. Swab cultures were positive in at least 1 sample in 55 (55%) patients and positive in 272 (45%) of 600 samples (Figure 1). The majority of cultured bacteria were Propionibacterium species (mainly P. acnes), which were detected in 249 (42%) swab cultures. Coagulase-negative Staphylococci (mainly S. epidermidis) were detected in 49 (8%) swab cultures. Coagulase-positive Staphylococci (S. aureus) were not detected in any swab culture.

No statistical difference between de novo implantations and replacements was detected in the positive ratio of the swab cultures for Propionibacterium species (45% vs. 47%, P=0.8) or for coagulase-negative Staphylococci (14% vs. 24%, P=0.1) (Figures 2,3). The positive ratio for any bacteria was not correlated with the number of previous device replacements (Figure 4).

**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, was not different...
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 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 between the patients with a de novo implantation and those with replacement at any of the 3 time points (Figure 6).

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.

Figure 4. Comparison in the ratio of positive culture among the patients with different numbers of previous device replacements. Device replacement is a known risk factor of infection, but in this study, the ratio of positive bacterial culture was not correlated with the number of device replacements. CNS, coagulase-negative Staphylococci.

Figure 5. Comparison of the ratio of positive culture at 3 sampling time points. The 1st time point was immediately after the creation of a new pacemaker pocket or removal of the old generator. The 2nd time point was after the connection of leads to the new generator. The 3rd time point was after pocket lavage. Although the ratio of positive culture increased significantly at the 3rd time point compared with the 1st time point, it was not statistically different between 1st and 2nd or 2nd and 3rd time points.
were skin flora. 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 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 over-estimated 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. 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 P. acnes had been cultured at the time of pacemaker replacement, coagulase-negative Staphylococci was cultured at the time of infection, a result that is consistent with the previous report by Mason et al., 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? Because approximately 70% of CIED infections have been reported as caused by coagulase-negative Staphylococcus (eg., S. epidermidis and S. aureus), we should reconsider whether cultured bacteria could truly cause clinical infection when other bacteria are detected.

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
Bacterial Culture of CIED

cleansing and debridement can prevent bacterial colonization proceeding to clinical infection.6,7 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 causing clinical infection 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%,8 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,9,10 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 contamination during operation rather than bacterial colonization.

Conflict of Interest
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