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Infections of implantable cardioverter-defibrillators: frequency, predisposing factors and clinical significance

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ABSTRACT

The prognosis for patients with ventricular arrhythmias has improved dramatically with the aid of implantable cardioverter-defibrillators (ICDs). Although infection is a serious complication that frequently causes dysfunction and loss of ICDs, the frequency, predisposing risk-factors, and clinical and microbiological features are only partially understood. This study describes a retrospective review of 423 procedures in 278 patients with ICD primary implants and replacements performed at a tertiary-care hospital. Generators were placed in either a pectoral (68%) or abdominal (32%) site, and electrodes were placed transvenously in 97% of the patients. Most (95%) interventions were performed in a one-stage procedure. Infection developed with ten (2.4%) implanted devices. Four cases occurred within 30 days of surgery ('early infections') and six occurred >1 month after surgery ('late infections'). In univariate analysis, factors associated with the development of an early infection were: two-stage surgery, a sub-costal approach, and abdominal generator placement. In patients with late infections, a significant association was found with trauma or decubitus ulcer in the generator area. Infection presented with local signs without systemic complications. Seven of the ten patients required complete removal of the system.

Keywords Implantable cardioverter defibrillator, infection, management, pacemaker, risk-factors, surgical technique

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INTRODUCTION

The use of implantable cardioverter-defibrillators (ICDs) has changed dramatically the prognosis for patients with life-threatening ventricular arrhythmias [1–3]. Improvements in surgical techniques and device design have contributed to gains in effectiveness and safety [4–6], and the use of ICDs has increased significantly during the last two decades [7,8]. Infection is an uncommon, but serious, complication of ICD implantation. Although still controversial, risk-factors associated with infection include two-stage surgery, placement of the device through a median sternotomy or thoracotomy, abdominally placed generators and battery replacement, as well as diabetes mellitus, advanced age, depressed immunity and primary bacteraemia [5–13]. Management of infection often requires complete removal of the system.

The purpose of the present study was to determine the frequency of ICD infection in a large cohort of patients in a single university hospital, and to assess the risk-factors, clinical presentation, management and outcome of patients with infected ICD systems.

PATIENTS AND METHODS

A retrospective review of the hospital charts of patients undergoing ICD generator implantation at a university-affiliated hospital in Madrid between February 1988 and December 2001 provided data for 278 patients who underwent 423 procedures (262 primary implants, 161 replacements). Patients had regular follow-up visits every 3–6 months, which included physical examination and checking of the ICD system. Infection was diagnosed by the attending physician if fever (> 37.8°C) or any sign of infection (warmth, erythaema, tenderness or purulent drainage) were observed around the ICD pocket or surgical wound. Infection was classified on the basis of the time of presentation as 'early infection' (within

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30 days of surgery) or 'late infection' (> 1 month following surgery). Patient data collected included gender, age, New York Heart Association (NYHA) functional status and systolic ejection fraction (measured by echocardiography, ventriculography, or both), underlying cardiopathy, predisposing factors for infection (neoplasia, diabetes mellitus, obesity, haemodyalisis and hypoalbuminaemia <3 g/dL), anticoagulation drugs, corticosteroid therapy and the presence of an acute infectious disease (defined as any infection different from the ICD infection that developed during the 4-week period preceding the implant). The length of hospitalisation and the need for electrophysiological study before implantation (and the time that elapsed between that procedure and the implant) were also reviewed.

Antimicrobial prophylaxis comprised either (A) penicillin plus gentamicin plus cloxacillin, (B) vancomycin for penicillin-allergic patients, or (C) cefalozin alone, with the precise regimen being determined by the responsible surgeon. All prophylactic regimens were administered intravenously from 1 h before surgery until 48 h afterwards.

ICD implants were performed in the operating room by a cardiovascular surgeon, with the surgery involving either (i) sternotomy or thoracotomy, followed by placement of epicardial electrodes with or without patch electrodes (between 1988 and 1991), or (ii) a transvenous procedure, with either a sub-costal or sub-clavicular approach (from 1991 onwards). Transvenous electrodes were introduced into the venous system by transcutaneous cannulation of the left sub-clavian vein or, if not possible, by the left cephalic vein, jugular vein or right sub-clavian vein. Electrodes were inserted into the right ventricular apex. Pulse generators were placed in the abdominal (sub-rectal) or thoracic wall (sub-pectoral or sub-cutaneous), tunnelling leads until the correct position was reached.

Statistical analysis

Statistical analysis was based on the total number of procedures. Data were expressed as percentages, means ± standard deviation (SD) and median ± interquartile range (IQR). Quantitative variables were analysed by the Kolmogorov-Smirnoff test to confirm normality of data. When normality was not shown, logarithmic transformation was performed. An unpaired Student's *t*-test was used to compare the differences in continuous variables, and the chi-square test (or Fisher's exact test, for variables having expected frequencies of ≤5) was used to compare the distribution of discrete variables. The results were analysed using SPSS v.9.0 software (SPSS Inc, Chicago, IL, USA). Statistical significance was set at $p < 0.05$.

RESULTS

Patients and procedures

In total, 423 procedures performed in 278 patients were reviewed (262 primary implants and 161 replacements). The main reason for replacement was to renew the battery. Patients were mainly male (85.6%), and had a mean age of 60 ± 13 years. NYHA functional classifications were: grade I (62%); grade II (33%); and grade III (5%). The mean systolic ejection fraction was 35 ± 14% (range 10–86). Ischaemic heart disease was the most prevalent underlying cardiopathy (63%), followed by idiopathic dilated myocardiopathy (45%), congestive heart failure (22.7%), atrial fibrillation (20.3%) and valvulopathy (18.4%). Eleven (3.9%) patients had metallic valvular prostheses.

Fifty-eight (13.7%) patients were diabetic, 25 (5.4%) had neoplastic diseases, and 21 (5%) were morbidly obese. Overall, 26% were receiving anticoagulant therapy. Only a few patients were receiving haemodialysis (0.7%), corticosteroid treatment (0.7%) or had hypoalbuminaemia (2.4%). Thirty-four (8.1%) patients had suffered from an acute infection within the 4-week period preceding the implant, with seven patients having concomitant bacteraemia.

Patients were hospitalised for a mean of 15 days (IQR, 5–30 days), as no patient was discharged until therapy was completed. The mean time that elapsed between the electrophysiological study and the surgical procedure was 5 days. Most patients were given prophylactic regimen A (77%), followed by regimens C (14%) or B (9%). Most ICDs were positioned transvenously. The main surgical approach was subclavicular (62.1%), followed by sub-costal (32.9%). Major surgery was performed in 21 cases (sternotomy for 19 patients and thoracotomy for two patients). Only three implants were performed by sternotomy after 1991, because of the need for simultaneous heart surgery (coronary artery bypass grafting (CABG) or ventricular aneurysm resection).

Vascular access was performed via the subclavian route (71.2%). No vascular access was required for 27.9% of surgical procedures. Therefore, the pulse generator was placed in the pectoral position for 289 (68.3%) patients and in the abdominal position for 134 (31.7%) patients. In all but 11 (2.6%) cases, the surgical procedure was performed in one stage. Finally, the replacement procedures involved renewal of the pulse generator in 152 of the 161 replacements; in 33 cases, only the lead system was changed.

Infection rate

Thirty-eight (13.7%) patients developed fever in the post-surgical period, and another 16 (5.8%)

patients developed haematoma within the generator pocket. Overall, ten (2.4%) of 423 procedures resulted in ICD infection in eight (2.8%) of 278 patients. One patient, who had five ICD replacements, had three non-consecutive infections.

Infections involved five primary implants and five generator replacements (p 0.4). Four cases were early infections, occurring a mean of 14 days (5–21 days) after surgery, and six cases were late infections, occurring a mean of 26 months (1.5–84 months) following the procedure. The most relevant findings of these cases are shown in Table 1.

Predisposing risk-factors

Among the clinical variables, no significant association was found with ICD infection. In particular, the presence of acute infection or bacteraemia before the ICD implant did not correlate with ICD infection. By univariate analysis, infection was observed more frequently in patients with two-stage surgery than in patients with one-stage surgery (OR 21.7; 95% CI 4.73–99.48; $p < 0.01$), in patients with a sub-costal rather than a sub-clavicular approach (OR 6.62; 95% CI 1.39–31.458; $p < 0.01$), and in patients with an abdominal generator site rather than a pectoral site (OR 5.03; 95% CI 1.32–19.16; $p < 0.04$).

Late infections were observed in three patients with traumatic injuries (direct trauma or surgical trauma) on the generator site preceding the development of infection. In another three patients, infection developed after ulceration of the skin and partial extrusion of the pulse generator. Both trauma ($p < 0.001$) and decubitus ulcer (OR 138.33; 95% CI 14.36–1332.59; $p < 0.001$) were associated with late-onset infections.

Microbial aetiology

Microorganisms were isolated from cultures of the wound or the pulse generator pocket (eight cases), purulent collection (two cases), and culture from the generator (two cases) or the leads (two cases). Blood cultures, when taken, were negative in the infected patients. Infection was monomicrobial in five cases: coagulase negative staphylococci ($n = 3$), *Staphylococcus aureus* ($n = 2$), and *Streptococcus agalactiae* ($n = 1$). Four infections were polymicrobial: *Escherichia coli*, *Klebsiella* spp. and other Gram-negative bacilli. No organisms were isolated from one patient (Table 1).

Clinical presentation

The main clinical symptoms were swelling and purulent discharge (five cases), followed by fever (four cases), erythaema (four cases), pain (four cases) and ulceration of the skin (three cases). No association was found between ICD infection and the presence of post-surgical fever or haematoma. There were no systemic complications, cases of endocarditis or deaths.

Management and outcome

Early-onset infections. Three patients were given antimicrobial therapy with cloxacillin or amoxycillin-clavulanate for 2 weeks with a favourable outcome; local signs of infection disappeared and no relapses occurred. One of these patients underwent heart transplantation, with a good outcome, 4 months after the episode of infection.

A fourth patient also received antimicrobial therapy, but relapsed twice; complete explantation of the system was needed to achieve a cure,

Table 1. Relevant characteristics of patients with ICD infection

	Gender	Time to infection	Generator site	Implant/ replacement	Surgery	Trauma/ decubitus	Surgical approach	Aetiology	Treatment	Outcome
1	F	Early	Abdominal	Implant	x 1	–	Transvenous	Gram-neg. bacilli	Antibiotic	Cured
2	M	Early	Pectoral	Implant	x 1	–	Transvenous	–	Antibiotic	Cured
3	M	Early	Pectoral	Implant	x 1	–	Transvenous	*Escherichia coli* + *Klebsiella* spp.	Antibiotic	Cured
4	M	Early	Abdominal	Implant	x 2	–	Thoracic	CNS	Antibiotic	Relapsed
5	M	Late	Abdominal	Replacement	x 1	Trauma	Transvenous	*Escherichia coli* + *Klebsiella* spp.	Ab + Surgery	Reimplanted
6	M	Late	Abdominal	Replacement	x 1	Trauma	Transvenous	CNS	Ab + Surgery	Reimplanted
7	F	Late	Abdominal	Replacement	x 1	Decubitus	Transvenous	*Streptococcus agalactiae*	Ab + Surgery	Reimplanted
8	M	Late	Abdominal	Replacement	x 1	Decubitus	Thoracic	CNS	Ab + Surgery	Reimplanted
9	M	Late	Abdominal	Implant	x 2	Trauma	Thoracic	*Staphylococcus aureus*	Ab + Surgery	Loss
10	M	Late	Abdominal	Replacement	x 1	Decubitus	Transvenous	*Staphylococcus aureus* + *Bacillus* spp.	Ab + Surgery	Reimplanted

F, female; M, male; CNS, coagulase-negative staphylococci; Ab, antibiotic.

in conjunction with a full course of vancomycin and gentamicin.

Late-onset infections. Six episodes were treated with prolonged courses of antimicrobial agents, but complete removal and subsequent replacement of the ICD was eventually required in each instance. Vancomyin plus gentamicin was the principal antibiotic regimen. One patient had three different episodes of infection associated with decubitus ulcers and trauma during a 10-year period.

DISCUSSION

The present study has some limitations. First, it was conducted over an extended period and multiple surgeons of variable training performed the ICD implants (i.e., the level of experience may have influenced the results). Second, the small number of infections associated with ICD infection makes the detection of differences among infected and non-infected patients difficult. However, despite these limitations, this study contributes to an understanding of the epidemiology and clinical and microbiological aspects of infections associated with ICDs.

The low overall infection rate of 2.4% (which was in the middle of the range of 0.2% to 7.2% reported previously [5–10]) precluded the finding of significant associations among patients. Remarkably, patients with diabetes mellitus, obesity or bacteraemia preceding implantation did not have a higher risk for infection. However, as noted previously, two-stage surgery, a sub-costal surgical approach, and abdominal generator placement, were all associated with an increased infection risk. Two-stage surgery may increase the risk for infection as much as 20-fold, as the surgical wound is not isolated completely from skin flora and secondary manipulation can occur. Fortunately, two-stage surgery is now performed rarely. Long subcutaneous tunnelling is needed to connect the leads with the generator for both the sub-costal approach and in cases where the generator is located on the abdominal wall, and therefore more trauma and manipulation occur [7,12]. In addition, abdominal generators are more bulky and heavier, leading to the possibility of erosion and ulceration of the generator pockets. Subcostal implantation has been gradually replaced since 1995 by the sub-clavicular approach, and is currently under-used.

In the present series, early infections were seen in only a few patients with primary implants. These ICD infections mimicked incidental uncomplicated surgical wound infections, were caused by skin contaminants, and were treated easily with antimicrobial therapy. Fortunately, these infections did not result in the loss of the ICD. In contrast, late infections had some distinctive features of interest. These infections were associated with replacements of the system, and all the patients involved had pulse generators placed in the abdominal wall. In addition, all cases had a history of previous trauma or decubitus ulcers at the generator site. It has been suggested previously that loss of skin integrity is a risk-factor for late-onset ICD infection [6,8,14]. All the patients with late-onset infections needed complete explantation of the system and the reimplantation of a new device after a prolonged course of antimicrobial therapy.

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