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Rising Rates of Cardiac Rhythm Management Device Infections in the United States: 1996 through 2003

To the Editor: Clinical indications for cardiac rhythm management devices (CRMDs) have expanded dramatically. The impact of this expansion upon rates of CRMD infection, a complication of device therapy that often requires system explantation (1), has not been clearly defined.

We hypothesized that the current growth in implantable cardioverter defibrillator (ICD) utilization would impact rates of CRMD infection, both by expanding and changing the demographics of the population at risk. We analyzed a nationally representative database to compare trends in rates of new CRMD implants with rates of hospitalization for CRMD infection. We also sought to define the rates of in-hospital mortality associated with such events.

We collected files from the National Hospital Discharge Survey (NHDS) from 1996 to 2003. Cases with a primary discharge diagnosis of pacemaker (PM) or ICD infection (International Classification of Diseases-9th Revision-Clinical Modification [ICD-9-CM] code 996.61) were identified. In addition, patients with device explantation (ICD-9-CM codes 37.77, 37.79, 37.89, or 37.99) and a primary discharge diagnosis of sepsis (ICD-9-CM code 038 or 785.59), bacteremia (ICD-9-CM code 790.7), endocarditis (ICD-9-CM codes 421.0, 421.9, or 424.90), cellulitis (ICD-9-CM code 682.9), or fever (ICD-9-CM code 780.6) were defined as having CRMD infection. New CRMD implantations were identified by ICD-9-CM procedural codes 377.0 to 377.6.

In order to determine the clinical predictors for in-hospital mortality among patients with CRMD infection, a control group with previously implanted PM or ICD who did not have CRMD infection was identified. This much larger group included patients with PM or ICD in situ (ICD-9-CM codes V45.01 or V45.02, respectively) who were discharged with diagnoses other than CRMD infection. Demographic factors were recorded. Other characteristics were identified, including presence of diabetes (ICD-9-CM codes 250.00 to 250.02 or 250.70 to 250.72), renal failure (ICD-9-CM codes 585, 593.9, or V56.0), and hospital size.

Univariate analysis was performed using 1-way analysis of variance for continuous variables and the chi-square test for categoric variables. Multivariate analysis using a binary logistic regression test was undertaken to determine the independent predictors of in-hospital mortality. Cases were weighed using the "weight" variable for derivation of national estimates according to the NHDS guidelines. A p value of <0.05 was considered statistically significant.

During the study period, there was a 49% rise in the number of new CRMD implantations in the U.S., from 159,585 in 1996 to 237,720 in 2003. Most of this increase was driven by ICD insertions (160% for ICDs vs. 31% for PMs); however, the absolute numbers of PM implantations remained higher (180,284 for PMs vs. 57,436 for ICDs in 2003). From 1996 through 2003, there were no significant changes in the demographic characteristics of patients receiving CRMD implantations except that the proportion of patients receiving an ICD increased significantly (14% in 1996 vs. 27% in 2003, $p < 0.001$).

In the same period, the number of hospitalizations with CRMD infection increased 3.1-fold (2.8-fold for PMs and 6-fold for ICDs). Comparing 1996 with 2003, the increase in numbers of CRMD-infection-related hospitalizations was 6,720 for PMs and 1,779 for ICDs. Thus numbers of CRMD-infection-related hospitalizations continued to increase out of proportion to rates of new device implants (Fig. 1).

Cardiac rhythm management device infection conferred a high in-hospital mortality rate (Table 1). After correcting for age, gender, race, hospital size, presence of diabetes mellitus or renal failure, CRMD infection increased the risk of in-hospital death more than 2-fold (odds ratio [OR] 2.41, $p < 0.001$). Predictors of death also included older age (OR = 1.63 per 20-year increase in age, $p < 0.001$) and the presence of renal failure (OR = 1.76, $p < 0.001$).

Device infection is an uncommon but devastating complication of CRMD therapy. We found that rates of hospitalization for CRMD infection increased faster than rates of CRMD implants from 1996 through 2003. This disproportionate increase is consistent with the findings of Cabell et al. (2) who demonstrated accelerating rates of cardiac device infections among Medicare beneficiaries from 1990 to 1999. Our current data further demonstrate that the increase in the risk of infection of CRMD devices is continuing at an accelerated rate.

Reasons for such a disproportionate rise in CRMD infection are not clear. The recent shift toward ICD utilization for primary prevention of sudden cardiac death may play a role, primarily due to the disadvantaged health status of such ICD recipients. Our data illustrate a dramatic rise in CRMD infection beginning in

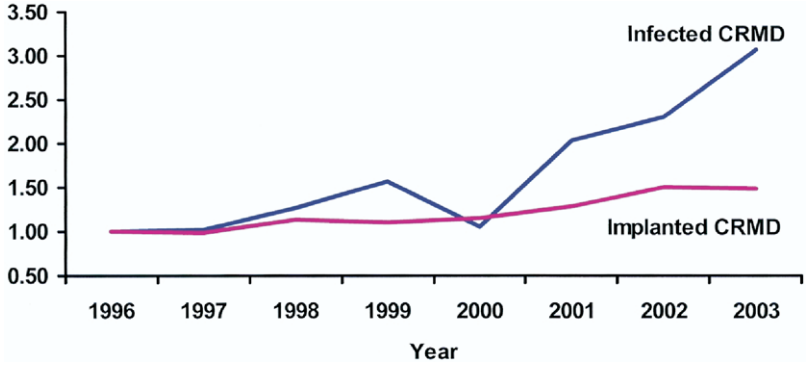

Figure 1. Proportional increase in the number of cardiac rhythm management devices (CMRD) implanted and those infected by the year of hospitalization, normalized to the number of devices implanted and infected in the year 1996, respectively. Note the dramatic increase in device infections compared with device implantations, particularly after the year 2000.

Table 1. Multivariate Predictors of In-Hospital Mortality in Patients With Cardiac Rhythm Management Devices

		95% CI		
	OR	Lower	Upper	p Value
Age per 20-yr increase	1.63	1.41	1.89	<0.001
Female gender	0.86	0.72	1.03	0.11
Race minorities vs. Caucasians	1.12	0.85	1.48	0.42
Diabetes mellitus	1.03	0.81	1.31	0.82
Renal failure	1.76	1.26	2.47	<0.001
Type of device implanted (ICD vs. PM)	0.78	0.55	1.11	0.17
Hospital size (per 100-bed increase in size)	1.04	0.97	1.12	0.26
CRMD infection	2.41	1.58	3.66	<0.001

CI = confidence interval; CRMD = cardiac rhythm management device; ICD = implantable cardioverter-defibrillator. OR = odds ratio; PM = pacemaker.

2001 and 2002, when early primary prevention ICD trials such as MADIT (Multicenter Automatic Defibrillator Implantation Trial) and MUSTT (Multicenter UnSustained Tachycardia Trial) were being digested and accepted by the scientific community. It remains unsettled, however, whether ICDs confer a higher infection risk than PMs (3,4). An indirect effect of expanding ICD indications could be an increased proportion of implantation by low volume operators or facilities, a factor that has been linked to higher rates of mechanical complications and infections (5). However, this probability cannot be tested using the NHDS database. It is also possible that greater physician awareness and improvements in detection and reporting of device-related infections have contributed to the rise over the study period. Regardless of the cause, the disproportionate rise in CRMD-related infections carries significant public health consequences, and further study is warranted to confirm this trend and to elucidate its causes.

In addition to its morbidity and associated additional health care resource expenditures, CRMD infection confers high in-hospital mortality rates. In the late 1990s, Chua et al. (6) retrospectively studied 117 patients undergoing device extraction for CRMD infection at a large tertiary care center and found low all-cause and zero-operative mortality. The recent expansion of ICD and cardiac resynchronization therapy to patient populations with a heavier burden of cardiovascular disease may explain the higher mortality seen with CRMD infection in this analysis.

This study has several important limitations. The NHDS database, though providing broad national representation, lacks detailed clinical information. Thus, determination of the mode of in-hospital death, the specialty of the implanting physicians, and the identification of the offending organisms are not within the scope of the NHDS. The validity of the data hinges upon appropriate coding of ICD-9-CM codes at the time of hospital discharge. We cannot exclude changes in coding patterns over the 8 years of the study period, for example to improve Medicare reimbursement for certain diagnoses. Because the NHDS records hospitalizations, but does not identify individual patients, the true incidence of CRMD infection cannot be determined.

In conclusion, our results demonstrate a rapid rise in rates of hospitalization for CRMD-related infection in the U.S. in the years 2001 through 2003, the last year for which data is currently available. This morbid and costly complication of CRMD therapy can be lethal, as evidenced by its associated high rates of in-hospital mortality. Further research should be undertaken to confirm these findings, determine the causes of rising rates of CRMD infections, and to improve therapeutic options for these important adverse events.

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Letters to the Editor

Questions in Cardiac Resynchronization Therapy: Metabolic Implications

With great interest we read the study by Bax et al. (1) relating to unresolved questions of cardiac resynchronization therapy (CRT). Many different trials have shown the beneficial effects of CRT using a variety of quantitative assessments such as the 6-min walk test, peak oxygen consumption (V_{O_2}), New York Heart Association (NYHA) functional class, quality-of-life measures, or mortality as primary end points. Among the exercise test variables, ventilatory efficiency (V_E/V_{CO_2}) slope is increasingly recognized as at least as good and possibly an even better prognostic indicator than peak V_{O_2} (2). Does CRT improve V_E/V_{CO_2} slope? So far only one uncontrolled study has addressed this question, and after 1 to 3 months no improvement was seen. A large body of evidence shows that chronic heart failure (CHF) affects skeletal muscle functional capacity and metabolic status (like increased insulin resistance [3]), which in turn contribute to patient symptoms. Information on changes of these parameters with CRT would be relevant in order to shed more light on the mechanisms of CRT-related improvement of symptomatic status. In CHF pa-