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16-Year Trends in the Infection Burden for Pacemakers and Implantable Cardioverter-Defibrillators in the United States

1993 to 2008

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Objectives We analyzed the infection burden associated with the implantation of cardiac implantable electrophysiological devices (CIEDs) in the United States for the years 1993 to 2008.

Background Recent data suggest that the rate of infection following CIED implantation may be increasing.

Methods The Nationwide Inpatient Sample (NIS) discharge records were queried between 1993 and 2008 using the 9th Revision of the International Classification of Diseases (ICD-9-CM). CIED infection was defined as either: 1) ICD-9 code for device-related infection (996.61) and any CIED procedure or removal code; or 2) CIED procedure code along with systemic infection. Patient health profile was evaluated by coding for renal failure, heart failure, respiratory failure, and diabetes mellitus. The infection burden and patient health profile were calculated for each year, and linear regression was used to test for changes over time.

Results During the study period (1993 to 2008), the incidence of CIED infection was 1.61%. The annual rate of infections remained constant until 2004, when a marked increase was observed, which coincided with an increase in the incidence of major comorbidities. This was associated with a marked increase in mortality and in-hospital financial charges.

Conclusions The infection burden associated with CIED implantation is increasing over time and is associated with prolonged hospital stays and high financial costs. (J Am Coll Cardiol 2011;58:1001–6) © 2011 by the American College of Cardiology Foundation

Implantation of cardiac implantable electrophysiological devices (CIEDs), which include permanent pacemakers (PM) and implantable cardioverter-defibrillators (ICDs), has dramatically increased over the past several years (1–3). This is largely due to the expanded indications for CIED implantation based on the results of large clinical trials of ICDs for primary prevention as well as the aging of the general population (4–6). Infection associated with CIEDs is a serious complication with high morbidity and mortality (7–9). Previous studies have suggested that the number of infections associated with CIEDs is increasing (10,11). We sought to analyze the historical trends for CIED infection in the United States over 16 years and evaluate the implications of these trends.

Methods

The Nationwide Inpatient Sample (NIS) discharge records were queried to identify demographic (e.g., age, sex), health profile/risk (incidence and severity of comorbidities, mortality), and health economic (length of stay, procedural costs and charges) data for PM and ICD patients between 1993 and 2008 using the International Classification of Diseases-9th Revision-Clinical Modification (ICD-9-CM). Specifically, procedures were identified by the ICD-9-CM codes that identified both primary and revision CIED procedures: Primary PM: 37.80–83, 00.50; Primary ICD: 37.94, 37.96, 00.51; PM Removal: 37.79, 37.85–87, 37.89, 00.53; ICD Removal: 37.98, 00.54. Revision procedures include pulse

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Abbreviations and Acronyms

CI = confidence interval
CIED = cardiac implantable electrophysiological device
HCUP = Healthcare Cost and Utilization Project
ICD = implantable cardioverter-defibrillator
ICD-9-CM = International Classification of Diseases-9th Revision, Clinical Modification
NHDS = National Hospital Discharge Survey
NIS = Nationwide Inpatient Sample
PM = pacemaker

generator replacement as well as device upgrades to either dual-chamber or cardiac resynchronization therapy devices. During this time period, the ICD-9-CM codes for these procedures have been consistent, thereby allowing the analysis of longitudinal trends in the data for prevalence of device implantation.

Patients with a CIED-related infection, either pocket infection or systemic infection including lead-associated endocarditis, were identified in 1 of 2 ways: 1) an ICD-9-CM diagnosis code for device-related infection (996.61) along with any CIED primary procedure or removal code; or 2) a CIED removal code (37.77, 37.7, 37.89, 37.99) along with evidence of systemic infection such as sepsis (038 or 785.59), bacteremia (790.7), or fever (780.6). Patient health profile was evaluated by coding for renal failure, heart failure, respiratory failure, and diabetes mellitus.

The CIED infection burden was calculated by dividing the number of device-related infections by the corresponding number of primary or revision procedures. Analyses of the NIS records with the relevant surgical codes were conducted using SAS (version 9.2, Cary, North Carolina). Hospital charges over the time period of this study were adjusted to the equivalent amount in January 2009 using the consumer price index for medical services published by the Bureau of Labor Statistics. Hospital cost estimates were converted from hospital charges by the "cost-to-charge" ratio provided by the HCUP. If a cost-to-charge conversion ratio was not available for a particular hospital, the average conversion ratio for hospitals in the same sampling strata was used. The sampling weights and the stratified sampling design of the NIS were taken into consideration when computing summary statistics and standard errors of these estimates. The number of surgeries performed for a particular demographic group is a positive integer and is assumed to follow a Poisson distribution. A regression model was used to estimate the surgery and infection rate, normalized by the size of the population, and evaluation of the calendar year trend. The surgery rate was adjusted by age, sex, race, and census regions to accommodate differences in the prevalence among demographic subpopulations. The infection burden and patient health profile were calculated for each year, and linear regression was used to test for changes over time.

Results

Trends in CIED infection. Between 1993 and 2008, over 4.2 million primary implantations of PM (3,204,700 records) and ICD (1,124,000 records) were identified using ICD-9-CM procedure codes. We found that the incidence of CIED implantation increased an average of 4.7% annually, and the overall CIED implantation increased by 96% from 1993 to 2008 (Fig. 1). The majority of this increase was due to the large increase in ICD implantation (504%) as pacemaker implantation increased by 45% during this time

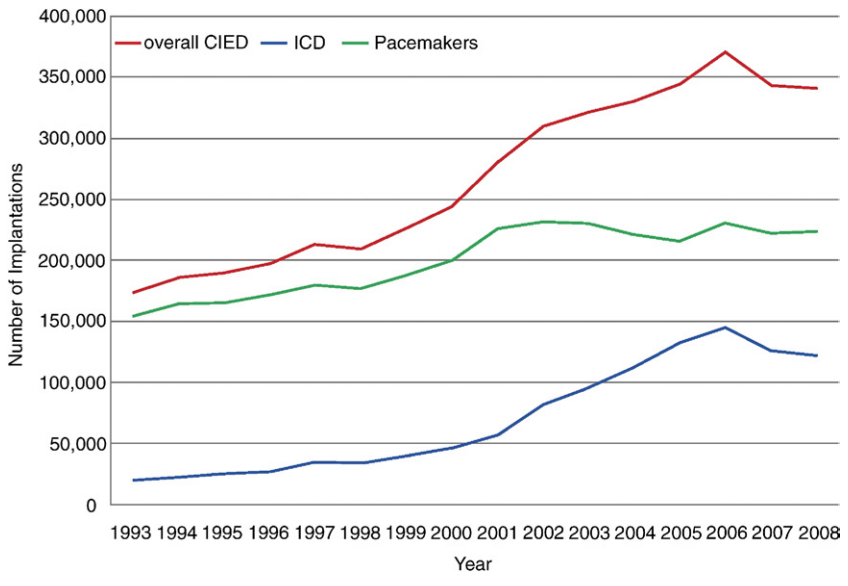

Figure 1 Annual Number of PM and ICD Implantations: 1993 to 2008

Between 1993 and 2008, overall cardiac implantable electrophysiological device (CIED) implantation increased by 96% (an average of 4.7%/year). Pacemaker (PM) implantation increased by 45%, whereas implantable cardioverter-defibrillator (ICD) implantation increased by 504%.

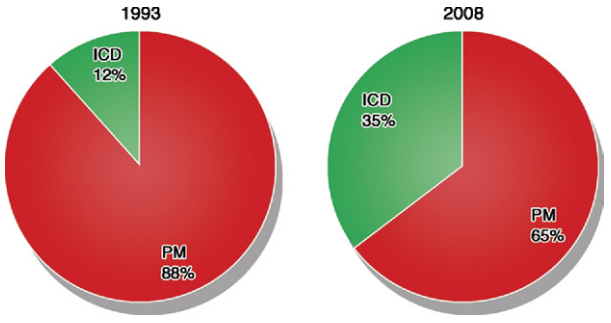

Figure 2 PMs and ICDs as a Percentage of All CIED Implantations: 1993 Versus 2008

The importance of the rise in ICD implantations is highlighted by the increase in 2008 to 35% of all CIED implants. Abbreviations as in Figure 1.

period. By 2008, ICDs represented 35% of all CIED implantations (Fig. 2).

During the study period (1993 to 2008), approximately 69,000 patients were treated for CIED infection (incidence = 1.61%). The incidence of infection increased by 210%, from 2,660 cases in 1993 to 8,230 cases in 2008. The annual rate of infections remained fairly constant until 2004 when a marked increase was observed. The rate of infection increased significantly, from 1.53% in 2004 to 2.41% in 2008 ($p < 0.001$) (Fig. 3).

The rates of CIED infection from 1993 to 2008, categorized by patient demographics (age, sex, race), showed that the highest infection rates occurred in patients that were white (82%), male (67%), and over the age of 65 years (64%) (Fig. 4).

Role of comorbidities in CIED infection. The incidence of 4 major comorbidities (renal failure, respiratory failure, heart failure, and diabetes) in patients with CIED infection remained fairly constant from 1993 through 2004 when a marked increase was observed (Fig. 5). In addition, the risk of mortality significantly increased in patients with respiratory failure (odds ratio: 13.58; 95% confidence interval [CI]: 12.88 to 14.3), renal failure (odds ratio: 4.28; 95% CI: 4.04 to 4.53), heart failure (odds ratio: 2.71; 95% CI: 2.54 to 2.88) but decreased slightly in patients with diabetes (odds ratio: 0.91; 95% CI: 0.86 to 0.96) ($p < 0.001$).

Financial burden and mortality rates associated with CIED infection. In 1993, in-hospital charges for CIED infection were approximately $75,000 and increased to over $146,000 by 2008, an increase of 47% per decade (Fig. 6). Inpatient mortality associated with CIED infection averaged 4.39%, but increased from 2.91% in 1993 to 4.69% in 2008, representing an increase of 1% per decade. During the study period, hospitalization remained constant and averaged 13.8 days.

Discussion

An analysis of the NIS demonstrates that during the study period 1993 to 2008, the national CIED infection burden increased. Specifically, there was an increase in the incidence of CIED infection along with an increase in inpatient

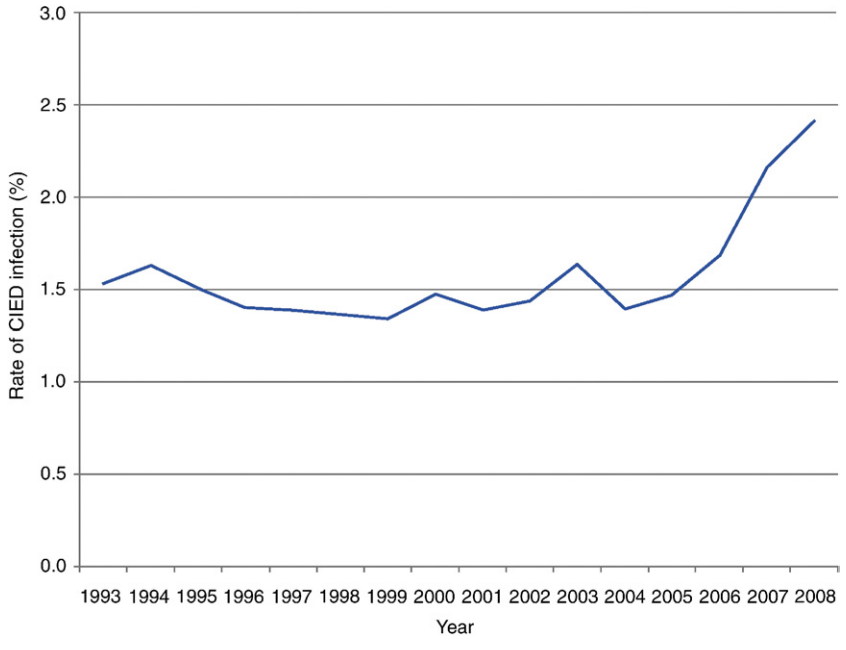

Figure 3 Rate of CIED Infection

The annual rate of cardiac implantable electrophysiological device (CIED) infection remained fairly constant until 2004 when there was a marked increase. The infection rate increased from 1.53% in 2004 to 2.41% in 2008 ($p < 0.001$).

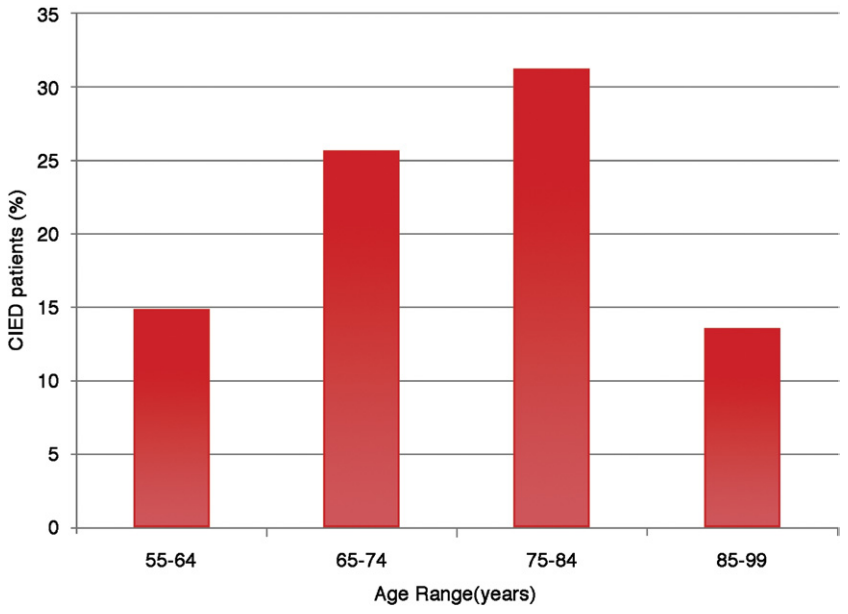

Figure 4 **Distribution of CIED Infection Based on Patient Age**

Cardiac implantable electrophysiological device (CIED) infections were more commonly observed in elderly patients.

mortality. Current patients have a high number of clinical comorbidities associated with prolonged hospital stays and an increase in the utilization of medical resources reflected by an increase in hospital charges.

Over the past 20 years, the number of patients with CIEDs has dramatically increased (1–3). Among Medicare beneficiaries, the rate of cardiac device implantation increased by 42% between 1990 and 1999 (10). Our initial

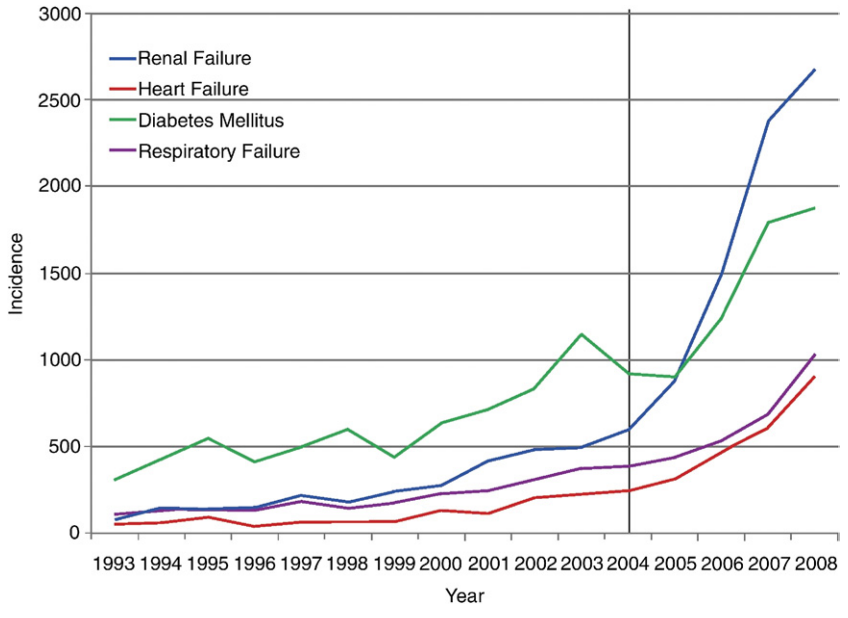

Figure 5 **Incidence of Comorbidities in Patients With CIED Infection**

The incidence of 4 major comorbidities (renal failure, respiratory failure, heart failure, and diabetes) remained fairly constant until 2004 when a marked increase was observed. This paralleled both the observed increase in implantable cardioverter-defibrillator implantation and the increased infection rate. CIED = cardiac implantable electrophysiological device.

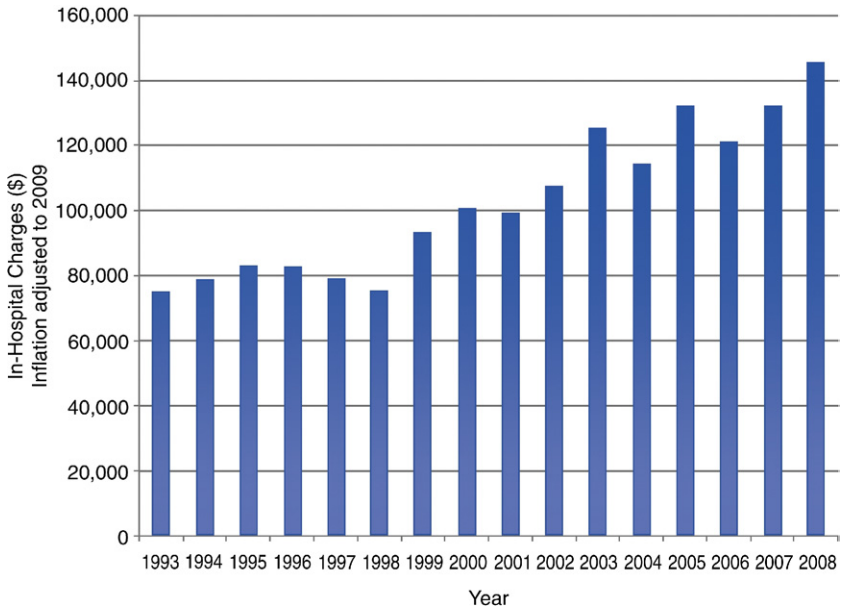

Figure 6 **In-Hospital Charges Associated With CIED Infection (Inflation Adjusted to 2009)**

The increased infection burden was associated with increased financial costs and higher inpatient mortality. In-hospital charges increased to over $146,000 by 2008, which represents an increase of 47% decade. CIED = cardiac implantable electrophysiological device.

analysis of NIS data, which included patients with all types of insurance coverage, showed a 30% increase in the primary pacemaker implantation rate of 50.0 per 100,000 persons of population in 1993 to 65.1 per 100,000 in 2006 (1). ICD implantation rate increased more rapidly during this period of time. In 1993, the ICD implantation rate was 6.1 per 100,000 persons of population and rose dramatically to 46.2 per 100,000 persons of population by 2006, an increase of over 500%.

The present study demonstrates that overall CIED implantation increased by 96%. Most of this increase was due to the marked increase in ICD utilization. By the end of the study period, ICDs represented 35% of all devices. It is estimated that CIED utilization will continue to grow over the next several years due to expanded Medicare coverage for these devices (12). Complications of CIED implantation are an important consideration in patient selection for CIED implantation. Interestingly, immediate post-procedural complications related to CIED implantation have decreased. Al-Khatib et al. (13) reported that the rate of post-procedural complications in CIED recipients fell between 2002 and 2005. The fall in procedure-related complications may be due to operator experience, improved device technology, and patient selection (13–15). Unfortunately, the corresponding risk of device-related infection has not changed during the same period of time (8,10,11,16,17).

Previous studies have attempted to define the burden of CIED infection. Voigt et al. (11) analyzed records from the National Hospital Discharge Survey (NHDS) between 1996 and 2006. Analysis of the NHDS database showed that device-related infection in CIED patients increased out of proportion to the overall increase in device utilization during the period 1996 to 2006. The NIS database, analyzed in the present study, samples about 25 times more discharge records than the NHDS and tends to sample data from larger institutions. This may account for some variation between the 2 surveys.

Results from our analysis of the NIS show that the annual incidence of CIED infection increased by 210% to 2.41% in 2008 ($p < 0.0001$). Our data may more accurately reflect the true CIED infection burden since previous studies may have included patients with infections of other cardiac devices such as prosthetic heart valves and not CIEDs alone. We required a CIED procedure code along with the 996.61 code to define a CIED infection. We also defined a device-related infection as evidence of sepsis or bacteremia along with a CIED removal code. This study and others highlight the disturbing trend of increasing CIED infection (8–11,16,17).

CIED infection is associated with high patient morbidity and a mortality rate of up to 18% (8,9,16,17). The financial burden of CIED infection is reflected by the 47% per decade increase in hospital charges related to CIED infection. By 2008, hospital charges were over $146,000. These expenditures do not include the additional costs of prolonged recovery and rehabilitation following treatment of the infection. Therefore, CIED infection has enormous economic implications (18).

The reason for the increasing rate of CIED infection despite a decrease in overall device-related complications is

not clear. One possibility for this observation includes the increasing numbers of ICD and cardiac resynchronization therapy devices whose longevity is significantly lower than PM. It is estimated that over 70% of ICD recipients will require device replacement surgery (19). Device replacement surgery is associated with an increased risk of infection (19,20). There may be an increasing burden of device replacements in the overall CIED population since ICDs now represent 35% of all implantations.

Patient characteristics, in addition to replacement burden, likely contribute to the increasing infection burden. It is well known that patients with chronic renal insufficiency and diabetes mellitus are at particular risk for CIED infection (21). Our analysis showed that there is an increasing incidence of these risk factors in CIED patients. Although the present study shows that the incidence of comorbidities in patients who present with CIED infection is increasing, it does not address the important question of what specific risk factors predict CIED infection or what factors might mitigate this issue. However, it does appear that patients with multiple comorbidities are at particular risk. Further study of these critical issues is important.

Conclusions

The infection burden associated with CIED implantation is increasing over time. This is likely due to expanding ICD indications and the increasing comorbidities in the CIED population. Infection is associated with prolonged hospital stays and high financial costs. Further investigation into the risk factors for CIED infection is warranted.

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