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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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Abstract

Objectives: We analyzed the infection burden associated with the implantation of cardiac implantable electrophysiologic devices (CIED) in the United States for the years 1993-2008.

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

Methods: The Nationwide Inpatient Sample (NIS) discharge records were queried between 1993-2008 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 (1993-2008), 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 co-morbidities. This was associated with a marked increase in mortality and in-hospital charges.

Conclusions: The infection burden associated with CIED implantation is increasing over time and is associated with prolonged hospital stays and high financial costs.

Abbreviations:

PM= Permanent pacemaker

ICD= Implantable cardioverter defibrillator

CIED= Cardiac implantable electrophysiologic device

ICD-9= 9th Revision of the International Classification of Diseases

NIS= National In-Patient Sample

CRT= Cardiac resynchronization therapy

Introduction

Implantation of cardiac implantable electrophysiology devices (CIED) which include permanent pacemakers (PM) and implantable cardioverter defibrillators (ICDs) has dramatically increased over the past several years.[1,2,3] 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.[4,5,6] Infection associated with CIEDs is a serious complication with high morbidity and mortality.[7,8,9] Previous studies have suggested that the number of infections associated with CIED is increasing.[10,11] We sought to analyze the historical trends for CIED infection in the United States over sixteen years and evaluate the implications of these trends.

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Methods

The Nationwide Inpatient Sample (NIS) discharge records were queried to identify demographic (e.g., age, gender), 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 1993-2008 using the 9th Revision of the International Classification of Diseases (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 generator replacement as well as device upgrades to either dual chamber or cardiac resynchronization therapy (CRT) 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 one of two ways: (1) an ICD-9 diagnosis code for device related infection (996.61) along with any CIED primary procedure or removal code, or (2) a CIED device 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). 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, and 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 1993-2008 (Figure 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 period. By 2008, ICDs represented 35% of all CIED implantations (Figure 2).

During the study period (1993-2008), approximately 69,000 patients were treated for CIED infection (incidence= 1.61%). The incidence of infection increased by 210% from 2660 cases in 1993 to 8230 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 ($p<0.001$) (Figure 3).

The rates of CIED infection from 1993-2008, categorized by patient demographics (age, gender, race), showed that the highest infection rates occurred in white (82%), male (67%) patients over the age of 65 (64%). (Figure 4).

Role of comorbidities in CIED infection

The incidence of four 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 (Figure 5). In addition, the risk of mortality significantly increased in patients with respiratory failure (odds ratio = 13.58; 95% CI 12.88-14.3), renal failure (odds ratio = 4.28; 95% CI 4.04-4.53), heart failure (odds ratio = 2.71; 95% CI 2.54-2.88) but decreased slightly in patients with diabetes (odds ratio = 0.91; 95% CI 0.86-0.96) ($p<0.001$).

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 (Figure 6). In-patient 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 Nationwide Inpatient Sample (NIS) demonstrates that during the study period 1993-2008, the national CIED infection burden has increased. Specifically, there has been an increase in the incidence of CIED infection along with an increase in inpatient 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.[1,2,3] Among Medicare beneficiaries, the rate of cardiac device implantation increased by 42% between 1990-1999.[10] Our initial analysis of NIS data[1] , 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. 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 device 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 and co-workers reported that the rate of post procedural complications in CIED recipients fell between 2002-2005.[13] The fall in procedure related complications may be due to operator experience, improved device technology, and patient selection.[13,14,15] Unfortunately, the corresponding risk of device-related infection has not changed during the same period of time.[8,11, 11,16,17]

Previous studies have attempted to define the burden of CIED infection. Voigt and colleagues analyzed records from the National Hospital Discharge Survey (NHDS) between 1996 and 2006.[11] 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 1996-2006. 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 two 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 CIED 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.[10,11,10,11,16,16]

CIED infection is associated with high patient morbidity and a mortality rate of up to 18%.[**Error! Bookmark not defined.**9,8,9,16] 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 CRT 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. While 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.

In summary, 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.

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

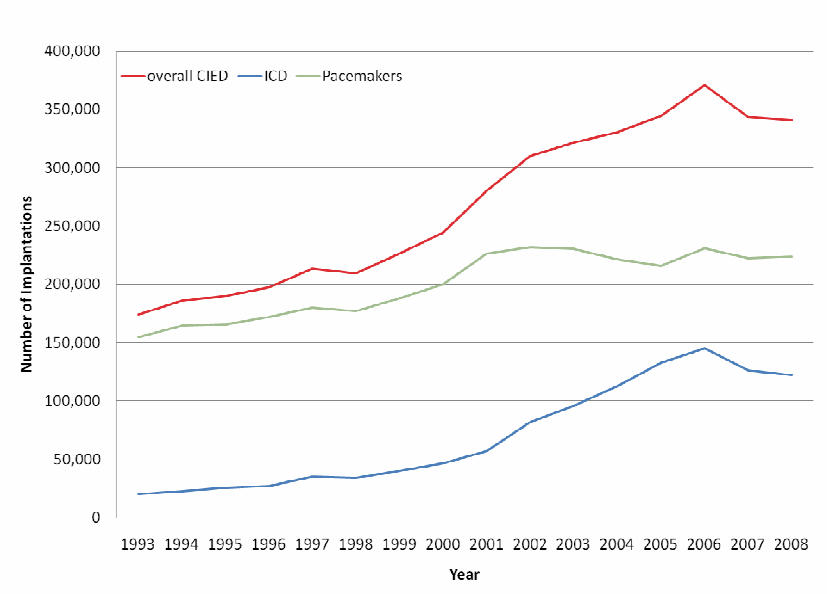


Figure 2. PMs and ICDs as a percentage of all CIED implantations: 1993 vs 2008

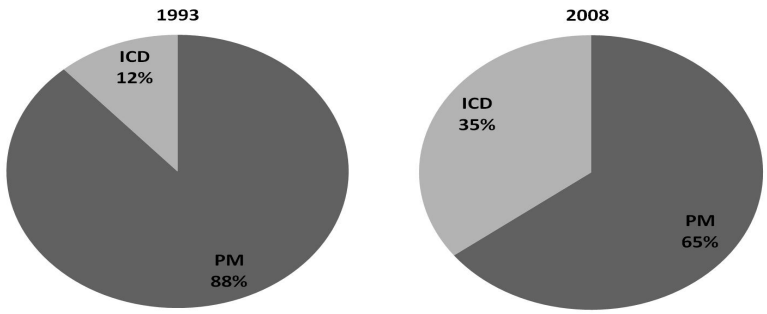


Figure 3. Rate of CIED infection.

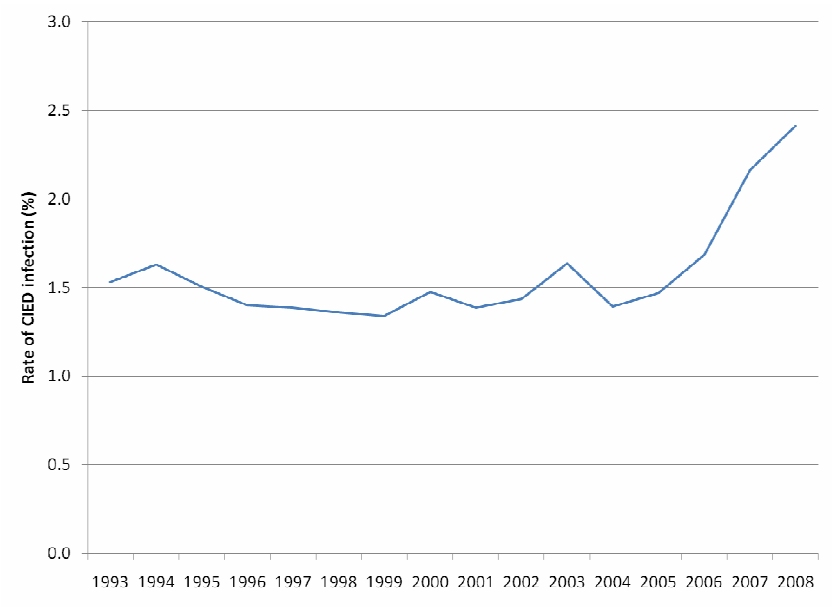


Figure 4. Distribution of CIED infection based on patient age.

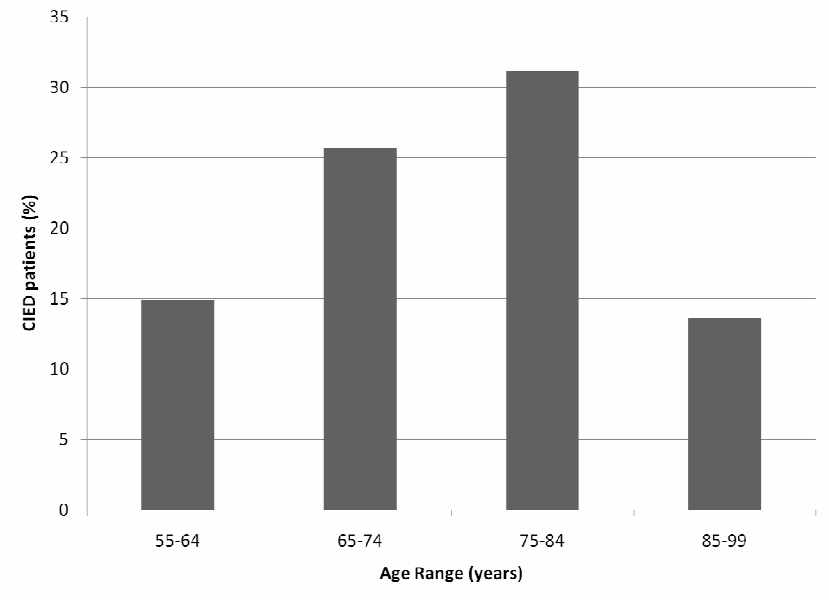


Figure 5. Incidence of comorbidities in patients with CIED infection

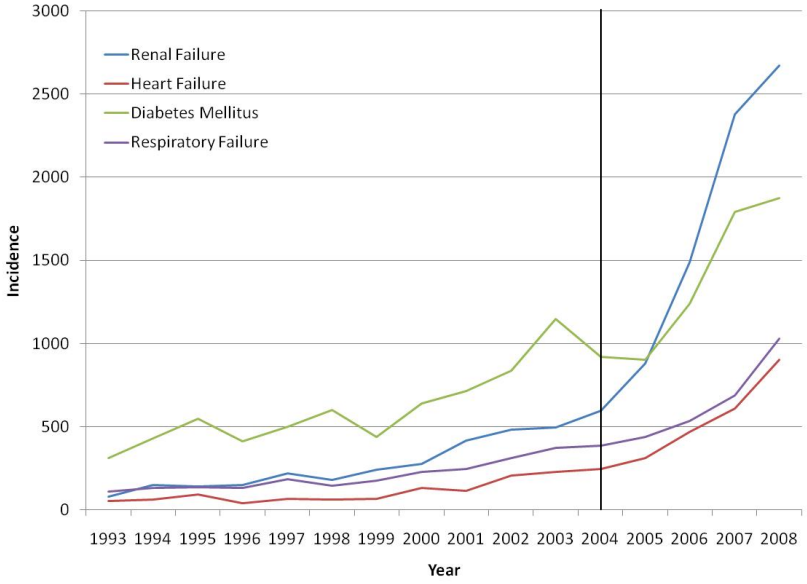
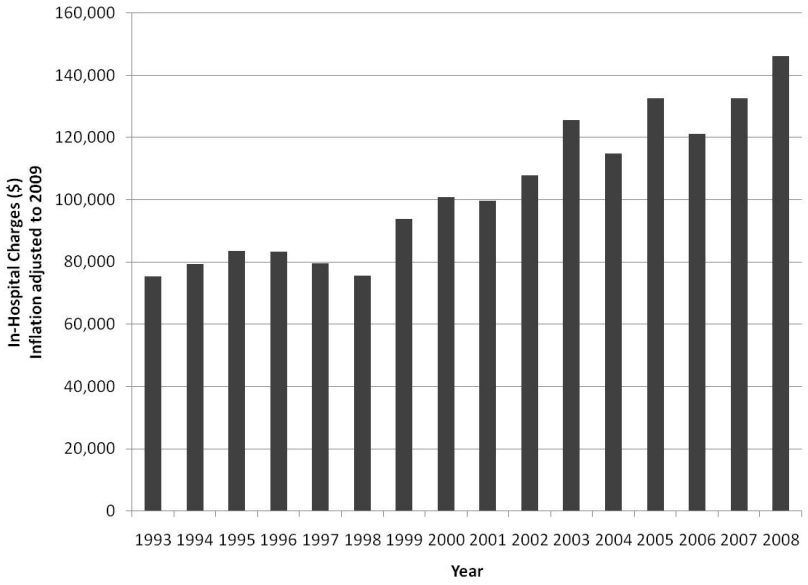


Figure 6. In-hospital charges associated with CIED infection (inflation adjusted to $2009)



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