Trends in the 30-year span of noninfectious cardiovascular implantable electronic device complications in Olmsted County

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BACKGROUND Cardiac implantable electronic devices (CIEDs), such as permanent pacemakers, implantable cardioverter-defibrillators, and cardiac resynchronization therapy devices, alleviate morbidity and mortality in various diseases. There is a paucity of real-world data on CIED complications and trends.

OBJECTIVES We sought to describe trends in noninfectious CIED complications over the past 3 decades in Olmsted County.

METHODS The Rochester Epidemiology Project is a medical records linkage system comprising records of over 500,000 residents of Olmsted County from 1966 to present. CIED implantations between 1988 and 2018 were determined. Trends in noninfectious complications within 30 days of implantation were analyzed.

RESULTS A total of 157 (6.2%) of 2536 patients who received CIED experienced device complications. A total of 2.7% of the implants had major complications requiring intervention. Lead dislodgement was the most common (2.8%), followed by hematoma (1.7%). Complications went up from 1988 to 2005, and then showed a downtrend until 2018, driven by a decline in hematomas in the last decade ($P < .01$). Those with complications were more likely to have prosthetic valves. Obesity appeared to have a protective effect in a multivariate regression model. The mean Charlson comorbidity index has trended up over the 30 years.

CONCLUSION Our study describes a real-world trend of CIED complications over 3 decades. Lead dislodgements and hematomas were the most common complications. Complications have declined over the last decade due to safer practices and a better understanding of anticoagulant management.

KEYWORDS Cardiovascular implantable electronic devices; Pacemaker; Implantable cardioverter-defibrillator; Cardiac resynchronization therapy; Complications

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Introduction

Cardiac implantable electronic devices (CIEDs) such as the permanent pacemaker (PPM), the implantable cardioverter-defibrillator (ICD), and cardiac resynchronization therapy (CRT) systems, are ubiquitously employed for managing a variety of cardiac arrhythmias and comorbidities. In recent years, we have witnessed an expansion in the indications for CIED implantation.[1–5] CIEDs have augmented patients' quality of life, reduced hospitalization length, and reduced mortality.[6–8]

Notwithstanding substantial technological improvements, complications involving CIED implants remain a significant issue.[9,10] Acute complications of CIED implants include lead dislodgement, perforation, pneumothorax, pocket hematoma, infection, and upper extremity deep vein thrombosis.[9–12] With an increase in life expectancy and expanding CIED implant indications, implantation-related adverse events are anticipated.[13,14] Device complications are critical to detect and manage to improve patient safety, prevent reoperations, reduce the length of hospital stay, and mitigate downstream healthcare costs.[15,16]

The majority of what we know about CIED complications is curated from secondary analysis of randomized trials,[10,17] registry-based studies,[18] or hospital-based databases.[19] Administrative claims–based databases have been shown to have low specificity in determining true CIED complications.[20] There exists a paucity of real-life population-based data on the incidence, trends, and predictors of CIED complications. Our group has previously published data on the trends of CIED infections.[14] In the present study, we present retrospective population-based data on the noninfectious mechanical CIED complications between 1988 and 2018.

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KEY FINDINGS

- Lead dislodgement stands as the foremost prevalent noninfectious complication post–cardiac implantable electronic device (CIED) implantation, followed by hematoma, pneumothorax, and cardiac perforation.
- Observations indicate a significant upward trajectory in overall complications from 1988 to 2005, which subsequently experienced a decline in incidence from 2005 to 2018, likely owing to better anticoagulation management.
- The spectrum and prevalence of comorbidities among patients undergoing CIED implantation have progressively escalated over time. The comorbidities of patients receiving CIED implants have steadily increased over time.
- The presence of prosthetic heart valves was an independent predictor of noninfectious complications, and obesity tends to confer a unique protective effect, consistent with the obesity paradox.

Methods

Data source

Our study was approved by the Mayo Clinic Institutional Review Board and received proper ethical oversight. Data were obtained from the Rochester Epidemiology Project (REP). The REP is a medical records linkage system containing medical records of all residents of Olmsted County, Minnesota, from January 1, 1966, to the present, consisting of follow-up data on more than 500,000 unique individuals. Patient demographics, diagnostic codes such as the International Classification of Diseases–Ninth Revision (ICD-9) and International Classification of Diseases–Tenth Revision (ICD-10) codes, and surgical procedure codes are recorded for all individuals. Paper and electronic medical records of these individuals are available for the generation of additional data. The REP permits the collection of population-based data and has been used to define the incidence of various medical conditions. It consists of 2 major hospital systems in Olmsted County (Mayo Clinic and Olmsted Medical Center) and smaller practices.

Study population

The REP database was used to determine all patients who received CIED implantation between 1988 and 2018. During the study period, Mayo Clinic and Olmsted Medical Center were the only 2 institutions in Olmsted County performing CIED implantation and follow-up. There were 4 device implanters in the early 1990s, and 10 in 2018 at Mayo Clinic, and Olmsted Medical Center had a single implanter from 2010 to 2015. Patients receiving CIEDs were determined based on ICD-9 Clinical Modification and ICD-10 Procedure Coding System codes. Data on subsequent device upgrades from PPM to ICD or CRT or ICD to CRT were collected using ICD-9 and ICD-10 codes and manually verified. For this study, we only included procedures that involved intracardiac lead implantation. Thus, subcutaneous ICDs, leadless pacemakers, generator change, and device extraction without lead implantation/revision were excluded. Data regarding baseline demographics and comorbidities were obtained from the REP and abstracted from the medical records. The patients' charts with device complications were manually reviewed to confirm the complications. The Charlson comorbidity index (CCI) is a score derived from multiple risk factors that predict 1-year survival and can be used as a surrogate for comorbidity. The CCI was calculated for all patients at the time of the CIED implantation. The unique complications were defined by a composite of ICD-9 and ICD-10 diagnosis codes, summarized in Supplemental Tables 1A–E. For lead dislodgement, we used codes for a lead revision within 30 days and confirmed lead dislodgement through manual chart review. The clinical definitions for postimplantation complications for this study are as follows. Notably, repeat surgical intervention was not a criterion to code the complications, and even those that were conservatively managed were included.

- Perforation: Any new pericardial effusion, with or without hemodynamic compromise.
- Hematoma: Any pocket bleeding that led to interruption of oral anticoagulant therapy or prolonged hospitalization >24 hours.
- Pneumothorax: Any pneumothorax detected on postprocedure chest radiography.
- Lead dislodgement: Included macro-dislodgement, as evident on a chest radiograph, and micro-dislodgement that were detected based on acute rise in capture thresholds.
- Major complications: Any complication as listed previously requiring repeat procedural intervention.

Statistical analysis

Normally distributed continuous variables were expressed as mean ± SD. The overall frequency of CIED complications was determined using the number of complications divided by the population at risk (device implants) in Olmsted County in the same period. Trends in complications over time, across age groups, and between genders were estimated using Poisson regression models. Comparisons between implant groups for categorical factors were completed using chi-square tests. Continuous factors were compared between groups using the analysis of variance. Overall survival was estimated using the Kaplan-Meier method. These curves were compared between groups using log-rank tests. P values $<.05$ were considered significant. All analysis was completed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Population characteristics

Between 1988 and 2018, there were 2536 CIED initial implants in Olmsted County, including 1927 PPMs (single

Table 1 Baseline demographics for all patients.

	Total (N = 2536)	No complications (n = 2379)	Complications (n = 157)	*P* value
Female	1068 (42.1)	994 (41.8)	73 (46.5)	.19
Age, y	73.9 ± 14.3	73.8 ± 14.3	74.8 ± 14.0	.39
Atrial fibrillation	1790 (70.6)	1677 (70.5)	112 (71.3)	0.80
CAD	1947 (76.8)	1802 (75.7)	118 (75.4)	.66
Cardiomyopathy	1166 (46.0)	1078 (45.3)	71 (45.2)	.94
Heart failure	1858 (73.3)	1741 (73.2)	116 (73.9)	.75
CKD	1287 (50.7)	1213 (51)	71 (45.2)	.17
COPD	950 (37.5)	890 (37.4)	67 (42.7)	.69
Diabetes	1580 (62.3)	1487 (62.5)	83 (52.9)	.01*
Heart transplant	40 (1.6)	38 (1.6)	2 (1.3)	.63
Hypertension	2206 (87.0)	2061 (86.6)	141 (89.9)	.18
Pulmonary hypertension	850 (33.5)	783 (32.9)	60 (38.9)	.17
Malignancy	1317 (51.9)	1232 (51.8)	83 (52.9)	.62
Obesity	1392 (54.9)	1322 (55.6)	69 (43.9)	.005*
TIA/stroke	843 (33.2)	781 (32.8)	61 (38.9)	.07
Valvular disease	1906 (75.2)	1766 (74.2)	127 (80.9)	.12
Prosthetic valve	436 (17.2)	393 (16.5)	40 (25.5)	.007*
Implant type				.89
CRT	169 (6.7)	157 (6.6)	12 (7.6)	
ICD	440 (17.4)	412 (17.3)	25 (16.0)	
Pacemaker	1927 (76.0)	1791 (75.3)	120 (76.4)	

Values are n (%) or mean ± SD.

CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; ICD = implantable cardioverter-defibrillator; TIA = transient ischemic attack.

*Indicates statistically significant differences ($P < .05$).

and dual chamber), 440 ICDs, and 169 CRT (pacemaker and defibrillator) devices. The mean age at device implantation was 73.9 ± 14.3 years. Women comprised 42.1% of all CIED recipients in the study (Table 1). A total of 174 complications were seen in 157 (6.2%) patients. Patients with CIED complications had a higher frequency of prosthetic valves and less frequency of obesity or diabetes. Of the 174 complications, there were 72 (2.8%) lead dislodgements, 44 (1.7%) pocket hematomas, 35 (1.4%) pneumothoraces, and 23 (0.9%) cardiac perforations (Table 2). Patients with cardiac perforation were more likely to be female and less likely to have cardiomyopathy (Table 3). There was a higher frequency of cardiomyopathy, prosthetic valves, and stroke in those patients who suffered pocket hematomas. Patients with pneumothoraces were older, more likely to be female, and less likely to have obesity or cardiomyopathy. There was no demographic predisposition to lead dislodgement.

Summary of complications

Of the patients with complications, 68 (2.7% of all implants) were classified as major complications requiring a procedural intervention. Seventeen patients experienced 2 complications, while the remaining 140 patients had only 1 complication each. Over three-quarters (n = 120 of 157) of the patients with complications had PPM implants. Sixteen percent (n = 25 of 157) of the patients with complications underwent ICD implantation, and the remaining 7.6% (n = 12 of 157) occurred in the CRT group. The complication rates in pacemakers, ICDs, and CRT devices were 7%, 6.4%, and 7.1% (P = NS).

Table 2 Distribution of the complications.

Complication	Number (% of total implants)
Lead dislodgement	72 (2.8)
Hematoma	44 (1.7)
Pneumothorax	35 (1.4)
Perforation	23 (0.9)

Among patients with complications, the median hospital stay following the CIED implantation procedure was longer at 3 (interquartile range [IQR] 2–5) days compared with a median of 1 (IQR 1–2) day in those without complications ($P < .01$). Out of 157 patients, 17.8% (n = 28) were diagnosed with complications postdischarge, with median occurrence on day 3 (IQR 2–14) following discharge. Additionally, 17.2% (n = 27) of patients required readmission to manage the complications.

Of the 23 (0.9%) patients who had perforations, about half (n = 12 of 23) required pericardiocentesis. Only 6.8% (n = 3 of 44) of the patients who developed hematomas required pocket re-entry to resolve the bleeding. The majority (88.7%) of the patients who developed hematomas were on either anticoagulation or antiplatelet medications or both, with 20.4% (n = 9 of 44) receiving periprocedural heparin (all before 2013). More than two-thirds (68.6% [n = 24 of 35]) of patients with pneumothoraces were managed conservatively, and the rest required chest tube placement temporarily before resolution. Of the 75 patients with lead dislodgement, 35 (46.7%) had atrial lead dislodgement, 35 (46.7%) had their right ventricular lead dislodged, and 5 (5.3%) had their coronary sinus lead dislodged. All 72

Table 3 Baseline demographics stratified by the type of complication.

	Perforation			Hematoma			Pneumothorax			Lead dislodgement		
	No (n = 2513)	Yes (n = 23)	*P* value	No (n = 2492)	Yes (n = 44)	*P* value	No (n = 2501)	Yes (n = 35)	*P* value	No (n = 2464)	Yes (n = 72)	*P* value
Female	1056 (42.0)	16 (69.6)	.009*	1055 (42.3)	16 (36.4)	.35	1042 (41.7)	19 (57.1)	.05*	1034 (42.0)	33 (46.7)	.42
Age, y	73.9 ± 14.3	76.4 ± 12.2	.34	73.9 ± 14.3	74.8± 15.0	.62	73.8 ± 14.3	78.3± 11.5	.04*	73.9 ± 14.3	73.3± 13.9	.72
Atrial fibrillation	1774 (70.6)	8 (34.8)	.21	1757 (70.5)	32 (72.7)	.86	1768 (70.7)	23 (66.7)	.57	1737 (70.5)	53 (74.7)	.43
CAD	1933 (76.9)	17 (73.9)	.74	1905 (76.7)	33 (75.0)	.67	1920 (76.8)	25 (73.8)	.65	1894 (76.9)	51 (72.0)	.32
Cardiomyopathy	1166 (46.4)	5 (21.7)	.01*	1137 (45.6)	32 (72.7)	.007*	1155 (46.2)	10 (31.0)	.05*	1130 (45.9)	35 (49.3)	.55
Heart failure	1847 (73.5)	15 (65.2)	.22	1820 (73.0)	37 (84.0)	.10	1830 (73.2)	27 (78.6)	.43	1806 (73.3)	51 (72.0)	.80
CKD	1282 (51.0)	9 (39.1)	.30	1264 (50.7)	23 (52.2)	.76	1270 (50.8)	15 (45.2)	.47	1256 (51.0)	31 (44.0)	.24
COPD	947 (37.7)	8 (34.8)	.66	929 (37.2)	22 (50.0)	.08	937 (37.5)	13 (38.1)	.93	926 (37.6)	25 (35.7)	.61
Diabetes	1570 (62.5)	14 (60.9)	.74	1555 (62.4)	23 (52.2)	.56	1565 (62.6)	1666 (47.6)	.05*	1542 (62.6)	38 (53.3)	.10
Heart transplant	43 (1.7)	0 (0.0)	.51	43 (1.7)	1 (2.3)	.86	40 (1.6)	0 (0.0)	.41	39 (1.6)	1 (1.9)	.86
Hypertension	2186 (86.9)	23 (100.0)	.04	2166 (87.0)	37 (84.0)	.97	2173 (86.9)	32 (92.9)	.25	2141 (86.9)	64 (89.3)	.54
Pulmonary hypertension	845 (33.6)	8 (34.8)	.70	833 (33.4)	19 (43.1)	.21	835 (33.4)	14 (40.5)	.34	825 (33.5)	23 (33.3)	.97
Malignancy	1309 (52.0)	11 (47.8)	.69	1291 (51.8)	32 (60.4)	.21	1293 (51.7)	22 (64.3)	.11	1283 (52.1)	34 (48.0)	.49
Obesity	1384 (54.9)	11 (47.8)	.75	1369 (55.1)	19 (43.1)	.09	1380 (55.2)	12 (35.7)	.01*	1355 (55.0)	36 (50.7)	.46
TIA/stroke	838 (33.2)	8 (34.8)	.67	813 (32.7)	23 (52.2)	<.001*	832 (33.3)	10 (31.0)	.75	818 (33.2)	23 (33.3)	.99
Valvular disease	1889 (75.1)	8 (34.8)	.23	1867 (74.9)	37 (84.0)	.1	1878 (75.1)	26 (76.2)	.88	1850 (75.1)	56 (78.7)	.48
Prosthetic valve	436 (17.3)	3 (13.0)	.74	424 (16.9)	16 (36.4)	.004*	432 (17.3)	4 (11.9)	.36	418 (17.0)	17 (24.0)	.11
Implant type			.04			.38			.64			.71
CRT	172 (6.8)	1 (4.3)		167 (6.7)	4 (9.0)		167 (6.7)	2 (7.1)		165 (6.7)	3 (5.3)	
ICD	445 (17.5)	0 (0.0)		432 (17.3)	10 (22.7)		435 (17.4)	4 (11.9)		428 (17.4)	10 (14.7)	
Pacemaker	1907 (75.8)	22 (95.6)		1897 (76.1)	29 (67.9)		1898 (75.9)	28 (81.0)		1870 (75.9)	57 (80.0)	

Values are n (%) or mean ± SD.

Abbreviations as in Table 1.

*Indicates statistically significant differences ($P < .05$).

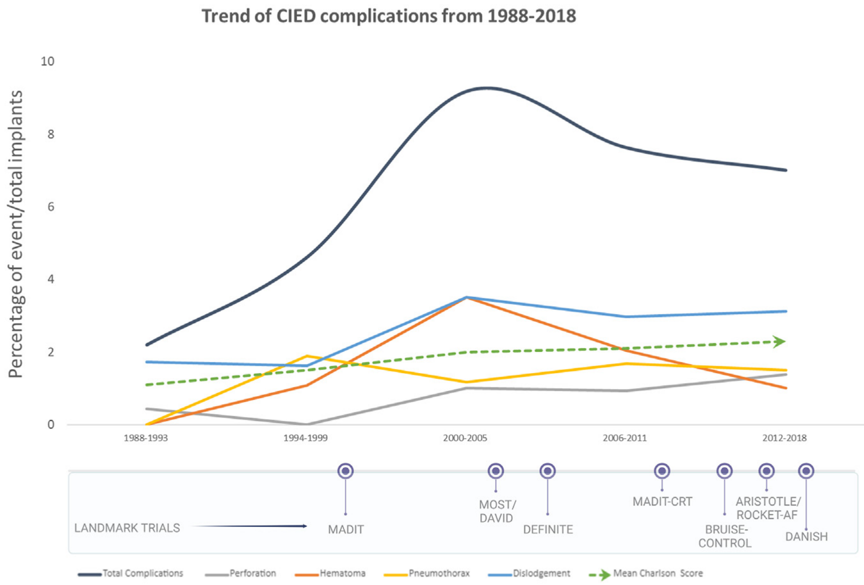

Figure 1 Trends of overall cardiac implantable electronic device (CIED) complications from 1988 to 2018. Trendlines are provided for perforations, hematomas, pneumothoraces, lead dislodgements, and the mean Charlson comorbidity indices. ARISTOTLE = Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation; BRUISE-CONTROL = Bridge or Continue Coumadin for Device Surgery Randomized Controlled Trial; DANISH = Danish Study to Assess the Efficacy of ICDs in Patients With Non-Ischemic Systolic Heart Failure on Mortality; DAVID = Dual Chamber and VVI Implantable Defibrillator; DEFINITE = Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation; MADIT = Multicenter Automatic Defibrillator Implantation Trial; MADIT-CRT = Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronization Therapy; MOST = Multi-arm Optimization of Stroke Thrombolysis; ROCKET-AF = Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation.

patients had their dislodged lead revised within a median of 1 (IQR 1–3) day after implantation.

Temporal trends in CIED complications

Temporal trends were compared between 5 intervals: 1988–1993, 1994–1999, 2000–2005, 2006–2011, and 2012–2018. There was a significant change in the proportion of complications over time (Figure 1). The total complications increased between 1988–1993 and 2000–2005, from 2.2% to 9.2%, and subsequently decreased to 7.0% in 2012–2018 ($P = .001$). Similar trends were noted for hematomas ($P < .01$). There were variations in the frequencies of patients with perforations, pneumothoraces, and lead dislodgement; however, these were not statistically significant.

In relation to total implantations, the percentage of pacemakers implanted has steadily declined over the years. The age- and sex-adjusted incidence of PPM implantation increased between 1988–1993 and 2000–2005, then decreased in 2012–2018. The age- and sex-adjusted incidence of ICD implantation increased between 1988–1993 and 2000–2005, then decreased in 2012–2018. In contrast, the age- and sex-adjusted incidence of CRT implantation continued to increase significantly from 2000–2005 to 2012–2018 (Figure 2A).[21] The complications trends showed an initial increase in these groups followed by a decline in more recent years, statistically significant within each group ($P < .05$) (Figure 2B).

Age and sex trends in CIED complications

When stratified by age, the percentage of implantations for all periods was the lowest in patients <50 years of age, higher in 50–70 years of age, and highest in patients >70 years of age ($P < .01$) (Figure 3A). The trend of complications in patients >50 years of age increased from 1988 to 2005 and then trended down ($P < .05$). In patients under 50 years of age, the frequency of the complications rose from 1988–1993 to 2000–2005, decreased in 2006–2011, and then increased again in 2012–2018, although it was statistically nonsignificant (Figure 3B).

Of the 157 patients with complications, 93 were men (53.1%), and 82 (46.9%) were women. Men have occupied a steadily growing percentage of the total implantations in every time period (Figure 4A). Within women, the complications increased from 1988–1993 to 2000–2005 and reached a plateau in recent years. In men, complications went up from 1988–1993 to 2000–2005 and then decreased until 2012–2018 ($P < .01$) (Figure 4B).

Trends in comorbidities and predictors of complications

Using the CCI, patients' comorbidities receiving CIEDs have increased over time (Table 4). However, there was no statistical difference between the CCI of patients with complications and those who did not within each time frame. When analyzed separately for each complication subtype, the only significant difference was noted in patients with hematoma from 2000 to 2011, who had higher CCI than those without (Supplemental Tables 2–5). When controlled for other factors, utilizing a multivariate regression model, the presence of prosthetic valves (odds ratio 1.62, 95% confidence interval [CI] 1.11–2.37, $P = .01$) was independently associated with a higher risk of noninfectious complications. Obesity was

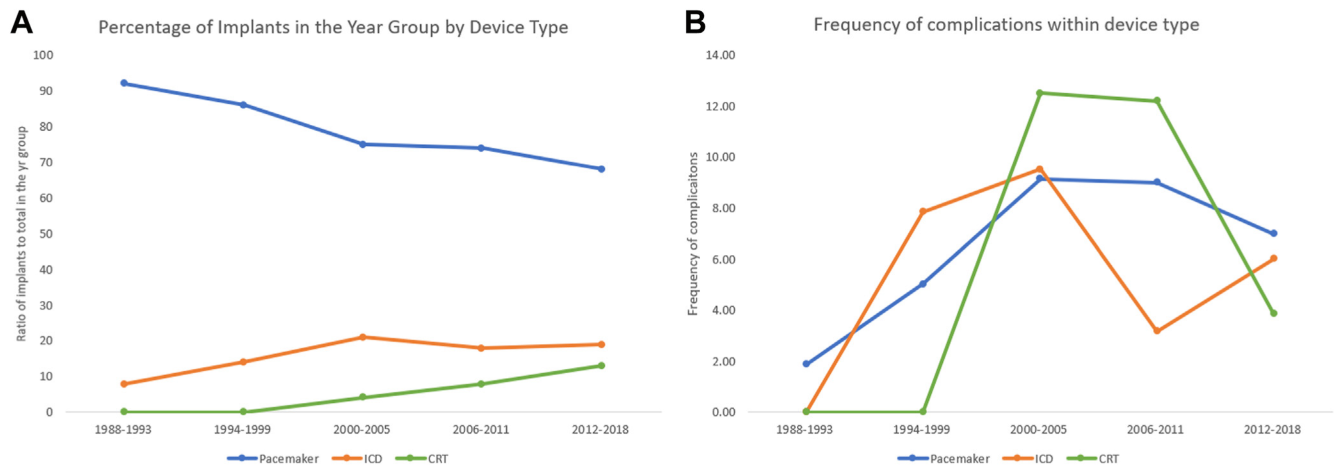

Figure 2 The trends of cardiac implantable electronic device complications by device type. (A) Percentage of cardiac implantable electronic device implants in the year-group by device type. (B) Frequency of complications within device type. CRT = cardiac resynchronization therapy; ICD = implantable cardioverter-defibrillator.

independently associated with a lower risk of noninfectious complications (odds ratio 0.68, 95% CI 0.40–0.95; P = .02) (Table 5).

Overall survival after CIED implantation

The median follow-up was 6 years (IQR 3.0–10.9 years). There were no deaths directly associated with the device complications. Survival after CIED complication was 63.2% at 5 years (95% CI 55.9%–70.4%) and 35.4% (95% CI 27.4%–43.4%) at 10 years, compared with 61.7% (95% CI 59.8%–63.6%) and 42.6% (95% CI 40.4%–44.8%), respectively, in patients without complications (P = .07) (Figure 5A). After PPM, ICD, and CRT implantation complications, the survival was 35.8% (95% CI 26.7%–44.9%), 38.2% (95% CI 18.9%–57.5%), and 15.6% (95% CI 0.0%–43.2%) at 10 years, respectively. In the PPM, ICD, and CRT implants without complications, the 10-year survival was 40.6% (95% CI 38.1%–43.1%, P = .25) 53.0% (95% CI 46.5%–58.55%, P = .10), and 43.5% (95% CI 33.0%–54.0%, P = .67) (Figure 5B–D). Women and men with a complication did not significantly differ in survival compared with those without (P = .21 and .20, respectively) (Figure 6).

Discussion

Using a large population-based record-linkage study, we describe trends in the noninfectious complications of CIED implantation. Our principal findings are the following. First, lead dislodgement is the most common noninfectious complication after CIED implantation, followed by hematoma, pneumothorax, and cardiac perforation. Second, the overall complications showed an upward trend from 1988 to 2005 and have reduced in frequency from 2005 to 2018. Third, the prevalence of complications is higher in patients over 50 years of age than younger patients. Fourth, the comorbidities of patients receiving CIED implants have steadily increased over time. Fifth, the presence of prosthetic heart valves was an independent predictor of noninfectious complications. Sixth, obesity tends to confer an independent risk reduction concerning noninfectious CIED complications. Last, long-term survival of patients with acute CIED complications was not different from those without complications but trended toward statistical significance.

Incidence of noninfectious complications

The overall incidence of acute (30-day) noninfectious complications after CIED implantations from 1988 to 2018 was

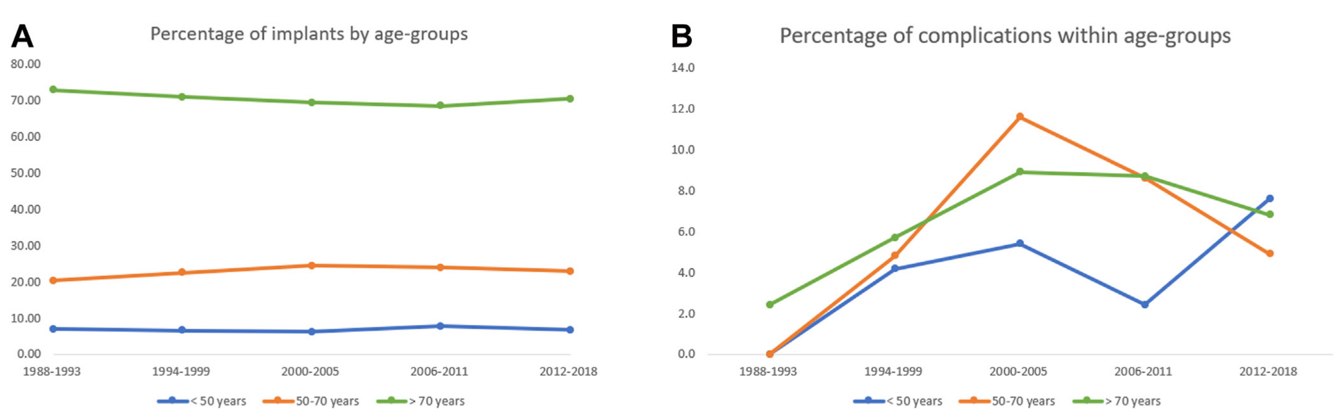

Figure 3 The trends of cardiac implantable electronic device complications by age. (A) Percentage of cardiac implantable electronic device implants in the year group by age groups. (B) Frequency of complications within age groups.

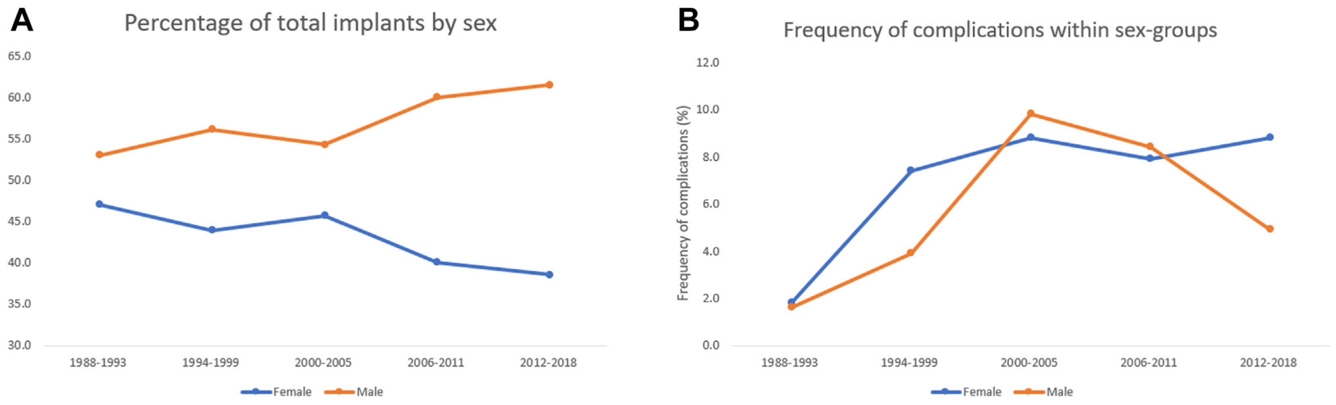

Figure 4 The trends of cardiac implantable electronic device complications by sex. (A) Percentage of cardiac implantable electronic device implants in the year group by sex. (B) Frequency of complications within sex groups.

estimated to be 6.2%, and that of major complications requiring intervention was 2.7%. Prior studies have shown wide variability in the percentage of complications (7%–18%) due to heterogeneity in study populations, the definition of complications, data sources, and follow-up duration.[10,12,22–24] Our findings seem to correlate with those reported by prior population-based studies.[22,25] However, there exists a discrepancy between the results of population-based studies, those obtained from administrative and claims databases,[12,26,27] those from the National ICD registry,[18,28] and those from large-scale clinical trials.[10,17]

While clinical trials are the gold-standard for assessing the effects of an intervention, the inclusion criteria are often quite strict, rendering a challenge in the generalization of observed events to the population.[29] Large-scale databases, while reflecting the real-world scenario, are fraught with issues regarding the accuracy of data and lack of detailed follow-up. Therefore, a population-based medical record linkage system such as the REP serves as an intermediary and is crucial for mitigating the limitations of alternative data sources. The definitions used in our study for the complications were more inclusive than prior studies, as our goal was to identify major and minor complications and their predictors.

Trends in device complications

Our group has previously described that the incidence of CIED implantations in Olmsted County increased gradually from 1988 to 2005. However, from 2005 to 2018, a decline in CIED implantations has been driven by a reduction in PPM and ICD implantations.[21] The overall trend of CIED complications has been similar, increasing from 1988–1993 to 2000–2005, followed by a downtrend until 2012–2018. The individual trends of lead dislodgement, hematoma, pneumothorax, and perforation followed the overall trends with slight variations when they peaked in the mid-2000s. While no prior studies have encompassed 3 decades of data, the trends seem to follow the most extensive reports from each period.[10,17,18,22,25,30] These data appear closely related to the previously described trends with infectious CIED complications.[14] The initial rise in complications seen from 1988 to 2005 reflects the increase in PPM in an aging population and expanding ICD indications for sudden death prevention, and the increase in the comorbidity burden.[14,21] Improved implantation techniques, use of micropuncture needles, and imaging-guided access, with better periprocedural anticoagulation strategies, may have contributed to the subsequent decline in complications.[31,32]

Table 4 Charlson comorbidity index trends from 1988 to 2018.

Year group	Complications	Patients analyzed	Overall mean Charlson comorbidity index*	Mean Charlson comorbidity index	P value†
1988–1993	No	225	1.1 ± 1.3	1.1 ± 1.3	.20
	Yes	4		0.3 ± 0.5	
1994–1999	No	338	1.5 ± 1.5	1.5 ± 1.6	.95
	Yes	16		1.6 ± 1.1	
2000–2005	No	525	2.0 ± 1.8	2.0 ± 1.8	.51
	Yes	51		2.2 ± 1.8	
2006–2011	No	470	2.1 ± 1.8	2.1 ± 1.8	.45
	Yes	39		1.9 ± 2.1	
2012–2018	No	729	2.3 ± 1.9	2.3 ± 1.9	.90
	Yes	47		2.3 ± 2.0	

Values are n or mean ± SD.
*The P value for the Charlson comorbidity index trend across all periods was significant at $<.01$.
†The P values described in this column are comparing patients with and without complication for each time period.

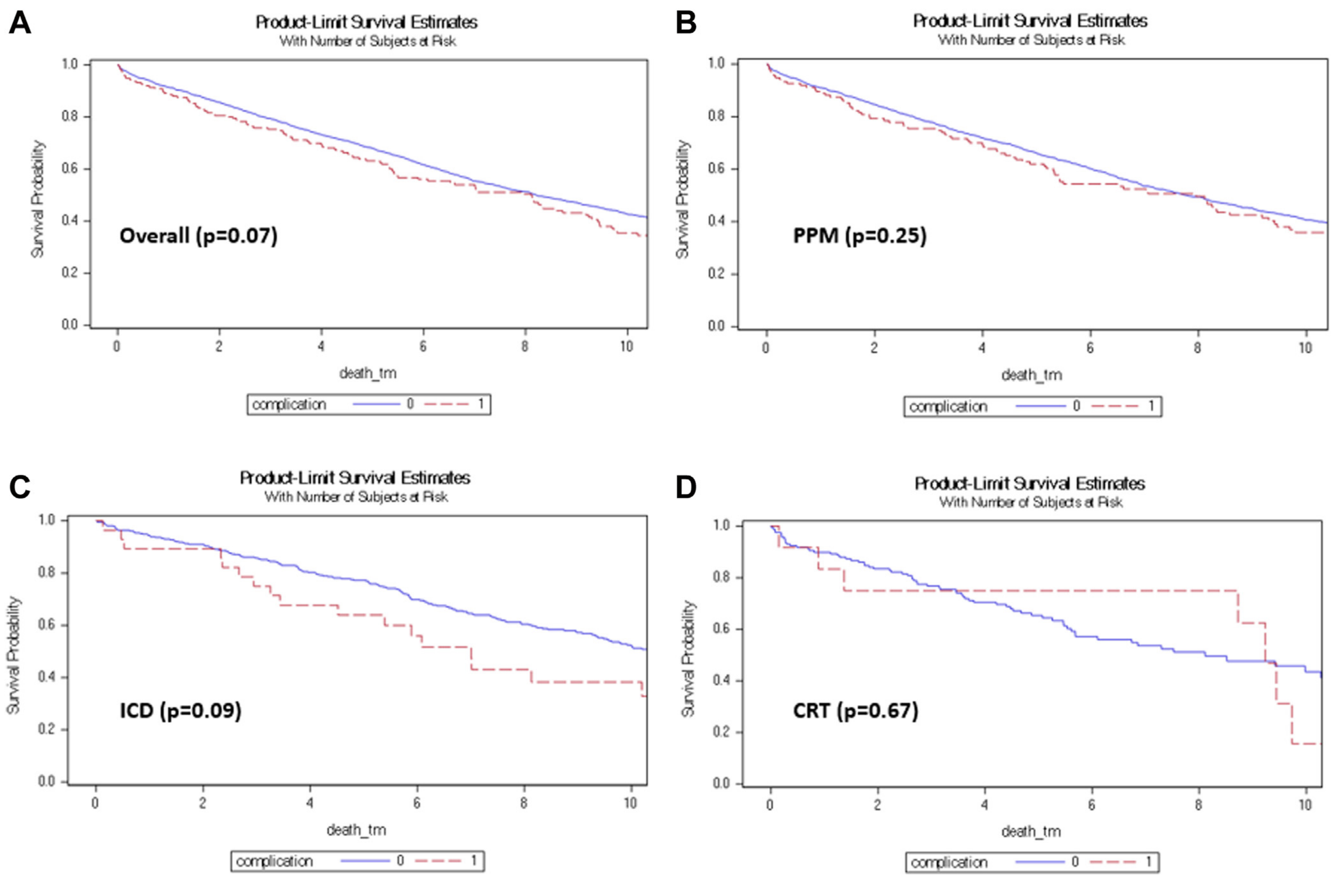

Figure 5 Survival curves in (A) the total population, (B) permanent pacemaker (PPM), (C) implantable cardioverter-defibrillator, and (D) cardiac resynchronization therapy based on the presence of complications or not. Abbreviations as in Figure 2.

Predictors of complications

Notably, the mean age of CIED implants at our institution was higher than in most prior population studies and trials.[14] Furthermore, our patients with 77% coronary artery disease, 75% valvular disease, 74% heart failure, 71% atrial fibrillation, and 62% diabetes mellitus, among others, represent a much sicker baseline population than prior studies.[18,19,22,23,33]

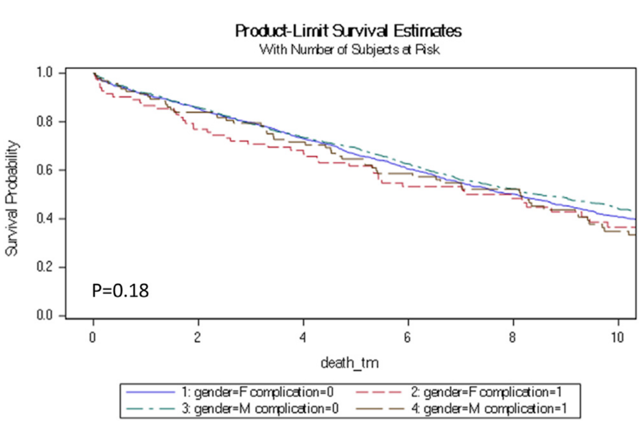

Figure 6 Survival curves by sex and complications. F = female; M = male.

The presence of prosthetic heart valves was an independent predictor of noninfectious complications after adjusting for other implicated factors in device complications. These could be attributed to longer procedure times due to intricate and complex anatomy and the higher propensity to be on anticoagulation. The incidence of hematoma was reduced after 2011, likely reflecting the advantage of uninterrupted oral anticoagulation, a lower risk of pocket bleeding compared with heparin bridging.[34]

Interestingly, obesity was shown to have an independent protective effect against noninfectious complications. The reverse epidemiology or obesity paradox is a well-established entity in chronic disease conditions and has recently been extrapolated to thoracic surgeries and CIED implantations.[35,36] Several mechanisms have been postulated to explain the obesity paradox, but the most relevant for CIED outcomes appear to be less cardiac cachexia, improved nutritional status, and better metabolic reserve with lower sarcopenia.[35,36] Obese patients tend to have a higher prevalence of comorbid conditions such as hypertension, diabetes, and sleep apnea that require closer periprocedural monitoring and may contribute to improved outcomes. This phenomenon is further evidenced by the extension of the obesity paradox to the critical care literature.[37] It is important to note that the protective effects of obesity are likely lost at extreme body

Table 5 Multivariate regression model for predictors of complications.

Variable	Odds ratio (95% confidence interval)	*P* value
Male	0.82 (0.60–1.14)	.24
Age at event	1.01 (0.99–1.02)	.44
Atrial fibrillation	0.99 (0.68–1.44)	.94
Diabetes	0.73 (0.53–1.02)	.06
COPD	1.11 (0.80–1.55)	.52
CKD	0.80 (0.57–1.12)	.20
Valvular disease	1.40 (0.91–2.13)	.12
Prosthetic valves	1.62 (1.11–2.37)	.01*
Obesity	0.68 (0.40–0.95)	.02*
PPM implant	0.91 (0.48–1.70)	.76
ICD implant	0.93 (0.46–1.90)	.85

PPM = permanent pacemaker; other abbreviations as in Table 1.
*Indicates statistically significant differences ($P < .05$).

mass indices (>40 kg/m^2), due to an increase in procedural time and complexity, with increased fluoroscopy duration.[22]

Survival after device implantation and sex considerations

Data regarding long-term survival after CIED complications are sparse. We found no significant difference in the 5- and 10-year survival in patients without acute noninfectious CIED complications compared with patients with complications, although there is a trend toward statistical significance.

Prior studies have shown that women are more likely to have short-term CIED complications.[22,38] While we saw a higher proportion of women in the patients that experienced a pneumothorax or perforation in our study, female sex was not an independent predictor of complications when adjusted for age and comorbid conditions. Additionally, women with acute CIED complications had no difference in long-term survival compared with men.

Limitations

Despite the benefits of having access to extensive population-based linkage data, our study has several limitations. Akin to any observational study, we cannot rule out the confounding effect due to unmeasured variables. Our sample consists predominantly of Caucasians, especially among the elderly. Prior studies have suggested that the data obtained from the REP could be generalized to a large percentage of the U.S. population. This may be inconsistent, especially when applied to populations with a higher proportion of ethnic minorities. We were also limited in using ICD codes for CIED implantation and CCI, which may have underestimated the actual counts of procedures and comorbid conditions. Yet, the number of CIED implantations is consistent with previous REP studies with manual verification of all implantations and complications.

Although our data are population based, most of the CIED-related care during the study period was provided by a single large tertiary hospital, which may have different practice patterns than community-based practices. While we understand that initial implants have a different risk profile than revisions, and generator replacements, we did not have a significant number of complications in lead revisions or device upgrades to make meaningful comparisons with de novo implants. Generator changes were not included in the study population.

Conclusion

CIED implantation complications cause morbidity and may require reintervention but are not associated with long-term mortality. The frequency of acute noninfectious complications has been gradually decreasing in recent years, likely owing to safer practices. Prosthetic heart valves appear to be an independent risk factor for complications, while obesity seems protective, supplementing the growing obesity paradox literature. Close monitoring of the trends and consistent vigilance would be needed to maintain the downtrend of CIED complications.

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Patient Consent: All patients provided written informed consent to participate in research.

Ethics Statement: Our study was approved by the Mayo Clinic Institutional Review Board and received proper ethical oversight. The research reported in this article adhered to the Helsinki Declaration guidelines.

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