ORIGINAL RESEARCH

Sex Differences in Acute Complications of Cardiac Implantable Electronic Devices: Implications for Patient Safety

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***Background*—**To date, limited population-level studies have examined the impact of sex on the acute complications of cardiac implantable electronic devices (CIED), including permanent pacemakers, implantable cardioverter defibrillators, and cardiac resynchronization therapy devices.

***Methods and Results*—**We studied all patients aged >18 years from 2010 to 2015 who were a resident of Australia or New Zealand, undergoing a new permanent pacemaker, implantable cardioverter defibrillator, or cardiac resynchronization therapy implant. Standardized variables were collected including patient demographic characteristics, primary and secondary diagnoses, procedures performed and discharge status. Diagnoses and procedures were coded as per the *International Classification of Diseases, Tenth Revision* (*ICD-10*) and the Australian Classification of Health Interventions. The primary end point was the incidence of major CIED-related complications in-hospital or within 90 days of discharge, with the effect of sex evaluated using multiple logistic regression. A total of 81 304 new CIED (61 658 permanent pacemakers, 12 097 implantable cardioverter defibrillators, 7574 cardiac resynchronization therapy) implants were included (38% women). Overall, 8.5% of women and 8.0% of men experienced a CIED complication (P=0.008). Differences between women and men remained significant after adjustment for age, procedural acuity, and comorbidities (odds ratio 1.10, 95% CI: 1.04–1.16, P<0.001). Differences in CIED complication rates were primarily driven by excess rate of in-hospital pleural drainage (1.2% women versus 0.6% men, P<0.001; adjusted odds ratio 1.86, 95% CI: 1.59–2.17, P<0.001) and pericardial drainage (0.3% women versus 0.1% men, P<0.001; adjusted odds ratio 2.17, 95% CI: 1.48–3.18, P<0.001).

***Conclusions*—**Women are at higher risk of acute CIED complications. Improvements in implant technique and technologies are required to minimize the risk of implant-related complications in women. **(*J Am Heart Assoc*. 2019;8:e010869. DOI: 10.1161/JAHA.118.010869)**

Key Words: complication • devices for heart failure • pacemaker • sex

Cardiac implantable electronic devices (CIEDs) including pacemakers (PPM), implantable cardioverter defibrillators (ICD), and cardiac resynchronization therapy (CRT), have grown to become an increasingly important component of clinical management in the past several decades. Despite the established presence of CIEDs in clinical practice, CIED implantation remains associated with a significant burden of complications associated with implantation.

In recent times, there has been a growing interest in the role of sex differences as a key determinant of safety outcomes in health care. To date, substantial evidence exists to demonstrate the association of sex differences with a

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Accompanying Tables S1 through S5 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.e010869

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Clinical Perspective

What Is New?

- Women have higher rates of overall complication within 90 days of cardiac implantable electronic device implantation.
- Acute pneumothorax and tamponade are twice as likely in women.

What Are the Clinical Implications?

- Use of ultrasound, or cephalic vein access in women may decrease risks of pneumothorax.
- Improvements in implantation technologies, such as improvements in lead technologies, may minimize risk of tamponade in women.

range of adverse outcomes in cardiac procedures including percutaneous coronary intervention (PCI)[1,2] and coronary artery bypass grafting (CABG)[3,4] and catheter ablation of atrial fibrillation.[5]

Thus far, limited population-level data exist on the influence of sex differences of overall CIED outcomes although several studies in the ICD populations have suggested a significantly higher prevalence of complications in patients who are women.[6,7] The current study seeks to extend beyond these previous studies by examining the influence of sex on acute complications in Australian and New Zealand patients undergoing new PPM, ICD, or CRT implants. The importance of including all CIED types is to enable determination of whether sex differences in complication rates is related to specific device type.

Methods

Data Source

Full access to all data was restricted to 1 author, who takes responsibility for its integrity and the data analysis. Access to deidentified data was approved by the human research ethics committees at state and national level across all included jurisdictions, with informed consent of subject waived. The data, analytic methods, and study materials are not available to other researchers for purposes of reproducing the results, as the authors are not permitted to release the data to third-parties for the conduct of research that would not be approved by the agencies that released the data.

We used hospitalization data from the Australian Admitted Patient Collection and New Zealand National Minimum Dataset (Hospital Events) which records patient encounters for all in-patient and day-only admissions from all public and most private sector hospitals and day procedure centers. Data were available from New Zealand (100% population) and 7 of the 8 Australian states and territories encompassing 99% of the Australian population (data were unavailable from the Northern Territory at the time of the analysis).

For each encounter, procedural data were collected using a standard set of variables including patient characteristics, primary and secondary diagnoses, all procedures performed and the patient status at discharge. In both Australia and New Zealand, diagnoses are coded as per the *International Classification of Diseases, 10th Revision*-Australian Modification (*ICD-10-AM*) and all procedures are coded per the Australian Classification of Health Interventions.

In Australia, patients' hospitalization encounters were linked to subsequent hospitalization and to each region's registry of deaths. Linkages of all health records were performed using probabilistic matching techniques based on multiple patient identifiers by designated data-linkage units within each region. In New Zealand, hospital encounters are linked nationally using a national unique patient identifier and all deaths are recorded in the National Minimum Dataset (Hospital Events).

Study Cohort

All patients aged >18 years undergoing a new PPM, ICD, or CRT implant (acute or elective) from 2010 to 2015 were included. The population was defined by Australian Classification of Health Interventions codes 38353-00 "insertion of cardiac pacemaker generator," and 38393-00 "insertion of cardiac defibrillator generator." Implantation of a left ventricular lead was used to identifying CIEDs with CRT capability. Implant codes are provided in Tables S1 and S2.

Patients were excluded for the following reasons: (1) CIED implant was a device replacement or upgrade; (2) patients undergoing CIED implantation during the same hospital admission as other procedures, eg, CABG, catheter ablation, because early complications could not be separated from the outcome of CIED implant-related events; (3) patients discharged against medical advice; (4) patients lacking at least 90 days of follow-up to allow post-discharge outcomes to be assessed.

Study Outcomes

The primary end point of the study was the composite of: (1) major in-hospital complications; and (2) major device-related complications occurring within 90 days of discharge.

In-hospital complications were defined as: (1) in-hospital death; (2) reoperation including (a) generator, lead or pocket reoperation including incision and drainage of hematoma, seroma, or abscess and (b) pericardial or pleural drainage; (3) post-procedural shock; and (4) infective endocarditis. Post-discharge complications included: (1) death within 30 days of

discharge; (2) reoperation including (a) device (generator, lead or pocket) including incision and drainage of hematoma, seroma, or abscess and (b) pericardial or pleural drainage; and (3) rehospitalization within 90 days with a primary diagnosis consistent with a device-related complication including (a) mechanical complication of the device; (b) infection (device infection, endocarditis, systemic infection); (c) complications relating to perforation and/or inflammation such as a pneumothorax or a pericardial effusion; (d) pocket-related complications such as hematoma or wound dehiscence; and (e) venous obstruction or thromboembolism and (f) other admissions for potentially serious device-related complications.

Minor complications managed without intervention such as small pneumothorax or effusion not requiring drainage were excluded from complications. All devices and outcomes were defined using diagnoses and procedure codes similar to definitions used in prior studies.[8,9] Prior studies of coding accuracy in the Australian setting have shown >85% accuracy for diagnoses and procedure coding with cardiovascular diagnoses and procedures being particularly well coded.[10] Outcome codes are provided in Tables S3 and S4.

Statistical Analysis

Data were summarized as frequencies and percentages for categorical variables. Continuous variables were presented as mean ± SD or as median and interquartile range. The frequency of early complication was calculated as the number of events divided by the number of patients and expressed as a percentage. Crude outcomes were compared by sex using Chi-square test or Fisher exact test as appropriate for categorical variables and the Students *t* test and the Mann–Whitney *U* test for continuous variables. The independent effect of sex on outcomes were assessed using logistic regression adjusting for differences in other patient characteristics associated with the outcome including patient age, acute or elective (planned) status of the procedure, device-type (PPM, ICD, CRT) as well as patients' comorbidities. Comorbidities were derived using the Condition Category (CC) classification system that is widely used to derive patient comorbidities from routinely collected hospital data.[11] The CC classification groups *International Classification of Diseases Tenth Revision-Australian Modification* (*ICD-10AM*) codes into ≈180 clinically meaningful conditions using diagnosis codes from the index admission and any hospitalizations in the preceding 12 months. To select comorbidities associated with the outcome, we first fitted a logistic regression model with all clinically relevant comorbidities. We then iteratively removed non-significant variables from the initial model using a stepwise purposeful selection approach described by Hosmer and Lemeshow.[12] Finally, to improve model fit, we evaluated clinically relevant interactions. The final model contained all variables significant at $P<0.05$ and interactions at $P<0.01$. The independent association of sex on all outcomes were reported as odds ratio (OR) with 95% CI with men as the referent group.

All significance levels were 2-sided with a $P<0.05$. All analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC). The Human Research Ethics Committees of the University of Adelaide and respective Australian states and territories provided ethical approval to undertake the study with a waiver of informed consent to use deidentified patient data. Data from New Zealand are obtained under a data user agreement with the New Zealand Ministry of Health and additional Human Research Ethics Committee approval was not required.

Results

Study Population

The characteristics of study patients are outlined in Table 1. A total of 81 304 patients with CIED implants were included (women n=30 840; 38%). CIED implantation was an acute procedure in 43% of women and 38% of men ($P<0.001$). Overall, women were older (women 76.5±12.4 versus men 73.7±12.3, $P<0.001$) and had a lower incidence of heart failure (women 19.4% versus 21.2%, $P<0.001$), ischemic heart disease (women 16.8% versus 27.2%, $P<0.001$) and diabetes mellitus (women 16.7% versus men 19.7%, $P<0.001$).

Overall Complications

Incidence of acute CIED complications are seen in Table 2. Overall, the primary study end point was reached in 8.5% of women versus 8.0% of men ($P=0.008$). Unadjusted risk of complication was higher in women compared with men for all CIED groups; PPM (women 7.9% versus men 7.4%, $P=0.01$), ICD (women 11.7% versus men 9.4%, $P<0.001$), and CRT (women 11.4% versus men 9.6%, $P=0.017$).

Adjusted odds ratios for acute complications for CIED overall can be seen graphically in Figure 1, and in tabular form in Table S5. After covariate adjustment, women experienced a higher overall rate of complication compared with men (OR 1.10, 95% CI: 1.04–1.16, $P<0.001$) with differences more pronounced in ICD (OR 1.25, 95% CI: 1.09–1.44, $P=0.002$) and CRT (OR 1.22, 95% CI: 1.04–1.43, $P=0.01$), with a trend towards increased complications in women in PPM (OR 1.06, 95% CI: 1.00–1.13, $P=0.06$). Breakdown of individual complications demonstrated that differences in the CIED complication rate was primarily driven by in-hospital reoperation rate (OR 1.23, 95% CI: 1.13–1.34, $P<0.001$), with women almost twice as likely to require pleural or pericardial drainage (OR 1.91, 95% CI: 1.66–2.21, $P<0.001$). Specifically, women had a

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Table 1. Patient Characteristics at CIED Implantation

	PPM (61 658)			ICD (12 097)			CRT (7574)			Overall (81 304)		
	Women (25 848)	Men (35 810)	*P* Value	Women (2542)	Men (9555)	*P* Value	Women (2450)	Men (5099)	*P* Value	Women (30 840)	Men (50 464)	*P* Value
Mean age, n (SD)	78.1 (10.9)	76.7 (10.6)	<0.001	61.1 (14.8)	63.8 (13.1)	<0.001	73.6 (12.6)	71.5 (11.8)	<0.001	76.4 (12.4)	73.7 (12.3)	<0.001
Length of stay, n (IQR)	4 (1–8)	3 (1–7)	<0.001	4 (1–12)	3 (1–11)	0.003	3 (1–8)	2 (1–7)	<0.001	4 (1–8)	3 (1–7)	<0.001
Acute procedure, n (%)	11 564 (44.7)	14 721 (41.1)	<0.001	832 (32.7)	3111 (32.6)	0.87	829 (33.8)	1393 (27.3)	<0.001	13 225 (42.9)	19 225 (38.1)	<0.001
Prior cardiac history												
Heart failure, n (%)	3930 (15.2)	4705 (13.1)	<0.001	1160 (45.6)	3926 (41.1)	<0.001	900 (36.7)	2042 (40.1)	0.01	5990 (19.4)	10 673 (21.2)	<0.001
Heart infection/inflammation, except rheumatic, n (%)	281 (1.1)	286 (0.8)	<0.001	68 (2.7)	172 (1.8)	0.005	36 (1.5)	69 (1.4)	0.69	385 (1.3)	527 (1.0)	0.007
Valvular and rheumatic heart disease, n (%)	1767 (6.8)	2113 (5.9)	<0.001	267 (10.5)	776 (8.1)	<0.001	233 (9.5)	445 (8.7)	0.27	2267 (7.4)	3334 (6.6)	<0.001
Hypertension, n (%)	8828 (34.2)	11 154 (31.2)	<0.001	782 (30.8)	3899 (40.8)	<0.001	844 (34.5)	1880 (36.9)	0.04	10 454 (33.9)	16 933 (33.6)	0.32
Specified heart arrhythmias, n (%)	5800 (22.4)	6294 (17.6)	<0.001	407 (16.0)	1728 (18.1)	0.01	523 (21.4)	1068 (21.0)	0.69	6730 (21.8)	9090 (18.0)	<0.001
Other heart rhythm and conduction disorders, n (%)	6462 (25.0)	8922 (24.9)	0.8	534 (21.0)	1994 (20.9)	0.90	538 (22.0)	1100 (21.6)	0.70	7534 (24.4)	12 016 (23.8)	0.05
Stroke, TIA, or cerebral hemorrhage, n (%)	699 (2.7)	1097 (3.1)	0.01	52 (2.1)	215 (2.3)	0.53	56 (2.3)	124 (2.4)	0.70	807 (2.6)	1436 (2.9)	0.05
Ischemic heart disease, n (%)	3808 (14.7)	7058 (19.7)	<0.001	811 (31.9)	4800 (50.2)	<0.001	559 (22.8)	1874 (36.8)	<0.001	5178 (16.8)	13 732 (27.2)	<0.001
PCI or CABG in the preceding year, n (%)	423 (1.6)	1095 (3.1)	<0.001	134 (5.3)	954 (10.0)	<0.001	81 (3.3)	324 (6.4)	<0.001	638 (2.1)	2373 (4.7)	<0.001
Comorbidities												
Major and metastatic cancer, n (%)	344 (1.3)	647 (1.8)	<0.001	27 (1.1)	93 (1.0)	0.70	31 (1.3)	55 (1.1)	0.47	402 (1.3)	795 (1.6)	0.002
Chronic lung disease, n (%)	1926 (7.5)	2897 (8.1)	0.004	271 (10.7)	1012 (10.6)	0.92	256 (10.5)	538 (10.6)	0.89	2453 (8.0)	4447 (8.8)	<0.001
Diabetes mellitus, n (%)	4290 (16.6)	6907 (19.3)	<0.001	444 (17.5)	1948 (20.4)	0.001	405 (16.5)	1072 (21.0)	<0.001	5139 (16.7)	9927 (19.7)	<0.001
Protein-calorie malnutrition, n (%)	1011 (3.9)	1266 (3.5)	0.02	77 (3.0)	243 (2.5	0.17	90 (3.7)	148 (2.9)	0.07	1178 (3.8)	1657 (3.3)	<0.001
Renal failure or dialysis, n (%)	2142 (8.3)	3245 (9.1)	<0.001	198 (7.8)	973 (10.2)	<0.001	218 (8.9)	638 (12.5)	<0.001	2558 (8.3)	4856 (9.6)	<0.001
Cellulitis, local skin infection, n (%)	524 (2.0)	763 (2.1)	0.38	39 (1.5)	182 (1.9)	0.22	38 (1.6)	97 (1.9)	0.28	601 (2.0)	1042 (2.1)	0.25

Normally distributed continuous variables are reported as mean with SD. Continuous variables that are not normally distributed are reported as median with 25th and 75th percentiles. Categorical variables are reported as absolute frequencies and percentages. CABG indicates coronary artery bypass graft; IQR, interquartile range; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

Table 2. Risk of Complications After CIED Implantation

Primary Outcome	PPM (61 658)			ICD (12 097)			CRT (7574)			Overall (81 304)		
	Women (25 848)	Men (35 810)	*P* Value	Women (2542)	Men (9555)	*P* Value	Women (2450)	Men (5099)	*P* Value	Women (30 840)	Men (50 464)	*P* Value
Composite device-related complications, n (%)	2052 (7.9)	2650 (7.4)	0.01	297 (11.7)	896 (9.4)	<0.001	279 (11.4)	490 (9.6)	0.02	2628 (8.5)	4036 (8.0)	0.008
In hospital complications												
Any in-hospital complication, n (%)	942 (3.6)	1094 (3.1)	<0.001	105 (4.1)	271 (2.8)	<0.001	116 (4.7)	182 (3.6)	0.01	1163 (3.8)	1547 (3.1)	<0.001
Deaths, n (%)	144 (0.6)	189 (0.5)	0.62	5 (0.2)	10 (0.1)	0.34	6 (0.2)	17 (0.3)	0.51	155 (0.5)	216 (0.4)	0.13
Reoperation, n (%)	801 (3.1)	910 (2.5)	<0.001	99 (3.9)	257 (2.7)	<0.001	110 (4.5)	162 (3.2)	0.004	1010 (3.3)	1329 (2.6)	<0.001
Lead operation, n (%)	414 (1.6)	567 (1.6)	0.86	46 (1.8)	163 (1.7)	0.72	59 (2.4)	(2.0)	0.30	519 (1.7)	834 (1.7)	0.74
Removal, n (%)	17 (0.1)	26 (0.1)	0.75	5 (0.2)	19 (0.2)	0.98	7 (0.3)	9 (0.2)	0.33	29 (0.1)	54 (0.1)	0.57
Replacement, n (%)	83 (0.3)	100 (0.3)	0.35	8 (0.3)	29 (0.3)	0.93	16 (0.7)	12 (0.2)	0.005	107 (0.4)	141 (0.3)	0.09
Revision, n (%)	329 (1.3)	458 (1.3)	0.95	35 (1.4)	118 (1.2)	0.57	40 (1.6)	84 (1.7)	0.96	404 (1.3)	660 (1.3)	0.98
Generator operation, n (%)	42 (0.2)	58 (0.2)	0.99	5 (0.2)	13 (0.1)	0.48	6 (0.2)	16 (0.3)	0.60	53 (0.2)	87 (0.2)	0.99
Pocket reoperation, n (%)	42 (0.2)	60 (0.2)	0.88	7 (0.3)	28 (0.3)	0.88	7 (0.3)	15 (0.3)	0.95	56 (0.2)	103 (0.2)	0.48
Pericardial/pleural drainage, n (%)	349 (1.4)	262 (0.7)	<0.001	43 (1.7)	66 (0.7)	<0.001	44 (1.8)	39 (0.8)	<0.001	436 (1.4)	367 (0.7)	<0.001
Pericardial drainage, n (%)	66 (0.3)	38 (0.1)	<0.001	8 (0.3)	6 (0.1)	0.00	5 (0.2)	5 (0.1)	0.31	79 (0.3)	49 (0.1)	<0.001
Pleural drainage, n (%)	294 (1.1)	228 (0.6)	<0.001	35 (1.4)	60 (0.6)	<0.001	39 (1.6)	35 (0.7)	<0.001	368 (1.2)	323 (0.6)	<0.001
Post-discharge complications												
Any post-discharge complication, n (%)	1161 (4.5)	1641 (4.6)	0.59	203 (8.0)	656 (6.9)	0.05	174 (7.1)	331 (6.5)	0.32	1538 (5.0)	2628 (5.2)	0.17
Deaths within 30 d, n (%)	185 (0.7)	272 (0.8)	0.53	17 (0.7)	33 (0.4)	0.02	22 (0.9)	37 (0.7)	0.43	224 (0.7)	342 (0.7)	0.42
Reoperation, n (%)	607 (2.4)	840 (2.4)	0.98	113 (4.5)	384 (4.0)	0.34	103 (4.2)	196 (3.8)	0.45	823 (2.7)	1420 (2.8)	0.22
Generator, n (%)	125 (0.5)	223 (0.6)	0.02	33 (1.3)	117 (1.2)	0.77	23 (0.9)	61 (1.2)	0.32	181 (0.6)	401 (0.8)	<0.001
Lead, n (%)	407 (1.6)	563 (1.6)	0.98	87 (3.4)	272 (2.9)	0.13	79 (3.2)	140 (2.8)	0.25	573 (1.9)	975 (1.9)	0.45
Pocket reoperation, n (%)	44 (0.2)	85 (0.2)	0.07	9 (0.4)	47 (0.5)	0.36	7 (0.3)	26 (0.5)	0.17	60 (0.2)	158 (0.3)	0.002
Pleural/pericardial drainage, n (%)	138 (0.5)	182 (0.5)	0.66	19 (0.8)	52 (0.5)	0.23	21 (0.9)	24 (0.5)	0.04	178 (0.6)	258 (0.5)	0.21
Pleural drainage, n (%)	43 (0.2)	30 (0.1)	0.003	9 (0.4)	11 (0.1)	0.02	5 (0.2)	7 (0.1)	0.54	57 (0.2)	48 (0.1)	<0.001

Continued

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Table 2. Continued

Primary Outcome	PPM (61 658)			ICD (12 097)			CRT (7574)			Overall (81 304)		
	Women (25 848)	Men (35 810)	*P* Value	Women (2542)	Men (9555)	*P* Value	Women (2450)	Men (5099)	*P* Value	Women (30 840)	Men (50 464)	*P* Value
Pericardial drainage, n (%)	104 (0.4)	155 (0.4)	0.56	12 (0.5)	45 (0.5)	0.99	16 (0.7)	17 (0.3)	0.05	132 (0.4)	217 (0.4)	0.97
Hospitalization for complications, n (%)	779 (2.9)	1052 (3.0)	0.58	145 (5.7)	483 (5.1)	0.19	114 (4.7)	231 (4.5)	0.81	1038 (3.4)	1766 (3.5)	0.31
Mechanical complication, n (%)	483 (1.9)	602 (1.7)	0.08	92 (3.6)	317 (3.3)	0.45	80 (3.3)	154 (3.0)	0.57	655 (2.1)	1073 (2.1)	0.98
Infection, n (%)*	139 (0.5)	248 (0.7)	0.02	34 (1.3)	99 (1.0)	0.20	20 (0.8)	54 (1.1)	0.32	193 (0.6)	401 (0.8)	0.006
Local perforation, n (%)†	60 (0.2)	76 (0.2)	0.60	5 (0.2)	19 (0.2)	0.98	9 (0.4)	5 (0.1)	0.02	74 (0.2)	100 (0.2)	0.21
Pocket complication, n (%)‡	53 (0.2)	93 (0.3)	0.17	7 (0.3)	40 (0.4)	0.30	6 (0.2)	24 (0.5)	0.14	66 (0.2)	157 (0.3)	0.01
VTE, n (%)	52 (0.2)	58 (0.2)	0.25	7 (0.3)	24 (0.3)	0.83	4 (0.2)	4 (0.1)	0.29	63 (0.2)	86 (0.2)	0.27

Continuous variables are reported as mean with SD. Categorical variables are reported as absolute frequencies and percentages. CRT indicates cardiac resynchronization therapy; ICD, implantable cardioverter defibrillators; VTE, venous thromboembolism.

*Infection includes device infection, endocarditis, or systemic infection.

†Local perforation includes admissions for perforation and/or inflammation such as a pneumothorax or a pericardial effusion.

‡Pocket complication includes hematoma or wound dehiscence.

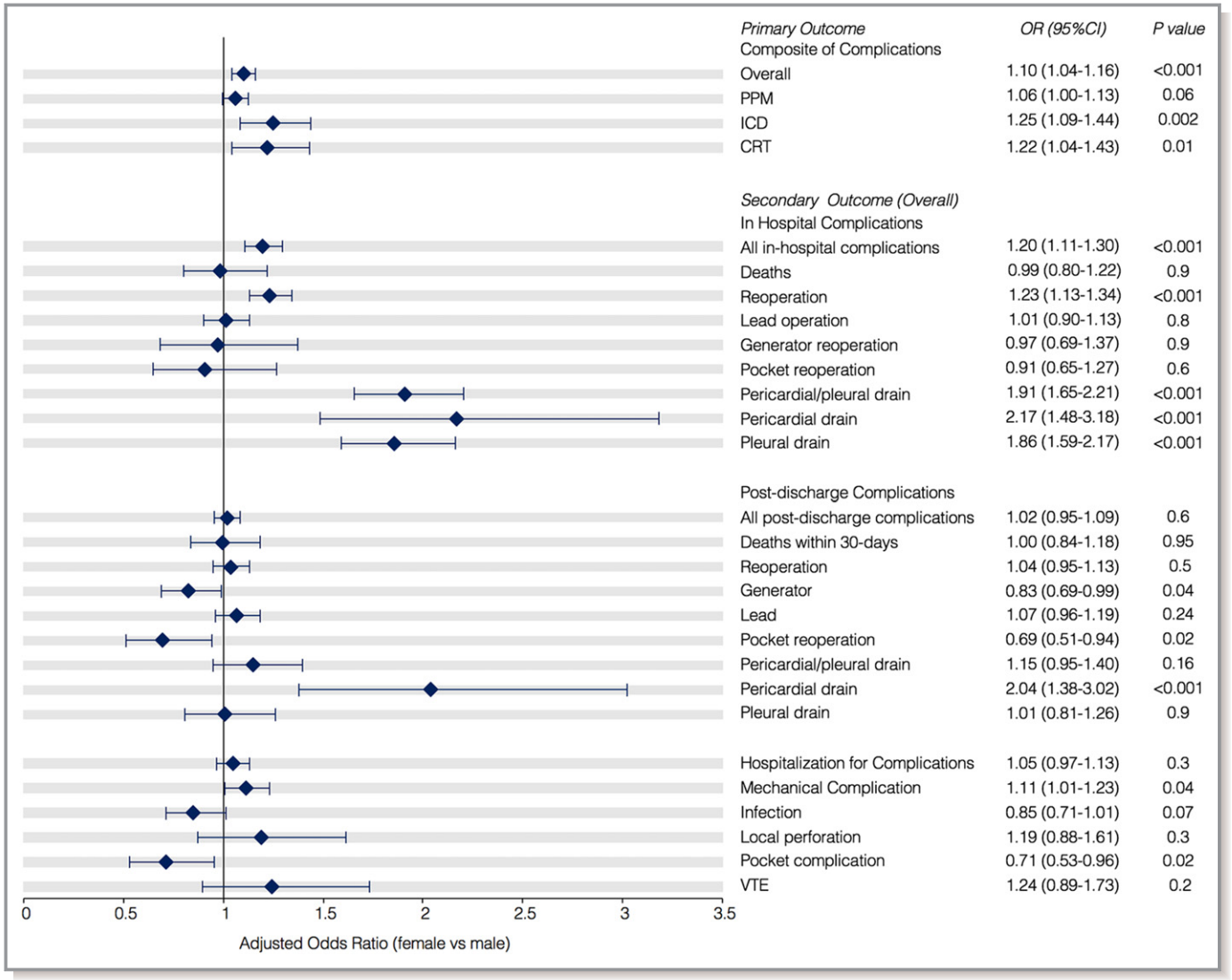

Figure 1. Adjusted risk of CIED complications for women vs men overall and by specific complications reported as adjusted odds ratio with 95% CI. CRT indicates cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; OR, odds ratio; PPM, permanent pacemaker; VTE, venous thromboembolism.

higher rate of pericardial drainage (OR 2.17, 95% CI: 1.65–2.21, $P<0.001$) and pleural drainage (OR 1.86, 95% CI: 1.60–2.17, $P<0.001$). Post-discharge incidence of pericardial drainage was also higher in women (OR 2.04, 1.38–3.02, $P<0.001$), however pleural drainage was equal between sexes.

Pericardial and Pleural Drainage

Figure 2 shows adjusted OR for in-hospital and post-discharge pericardial and pleural drainage for each device type. Sex difference for in-hospital composite pleural or pericardial drainage was most pronounced in the ICD (OR 2.34, 95% CI: 1.58–33.47, $P<0.001$) and CRT groups (OR 2.31, 95% CI: 1.49–3.60, $P<0.001$), compared with PPM (OR 1.81, 95% CI: 1.54–2.14, $P<0.001$). When considered separately, in-hospital pleural drainage was significantly higher in women for all device types, but more so for the ICD (OR 2.12, 1.39–3.23, $P<0.001$) and CRT (OR 2.29, 1.44–3.64, $P<0.001$) groups. Adjusted ORs for pericardial drainage for CRT and ICD groups could not be reported because of the low event rate. Post-discharge, women similarly experienced higher rates of pericardial drainage for PPM (OR 1.99, 1.25–3.19, $P=0.004$), as well as for pleural drainage for the CRT group (OR 2.05, 1.03–4.10, $P=0.04$), but not ICD or PPM groups.

Complications of Elective Procedures Only

Complication limited to elective procedures is shown in Figure 3. OR for composite early device-related complications

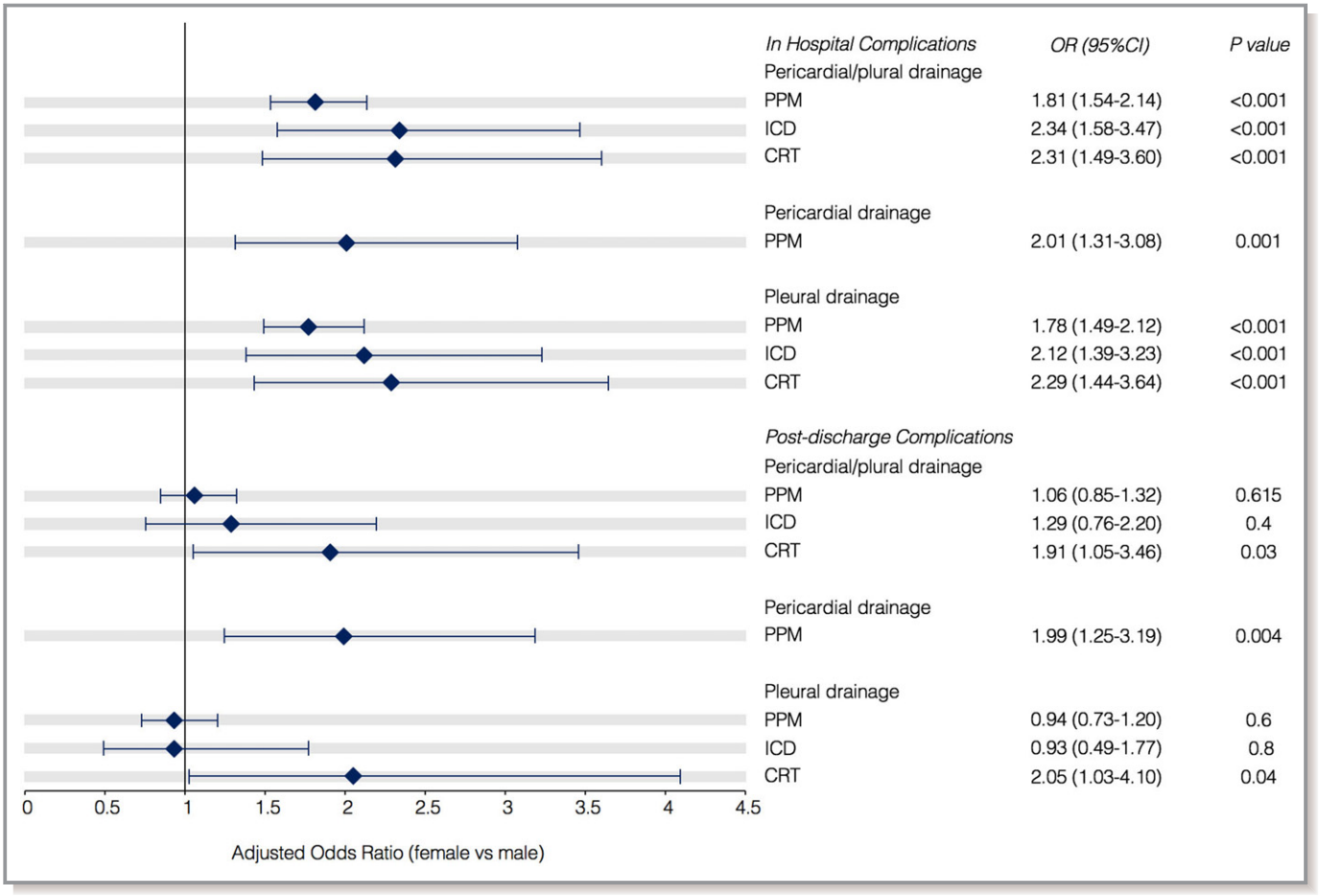

Figure 2. Pleural and pericardial drainage for CIED type reported as adjusted odds ratio with 95% CI, NB, Risk-adjusted in hospital and post-discharge pericardial drainage could not be reported for CRT and ICD groups because of low event rate. CRT indicates cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; PPM, permanent pacemaker.

is increased in women for all device types (PPM OR 1.13, 95% CI: 1.04–1.23, P=0.004; ICD OR 1.26, 95% CI: 1.07–1.52, P=0.006; CRT OR 1.25, 95% CI: 1.04–1.53, P=0.02). Women were significantly more likely to require in-hospital pericardial drainage (OR 2.71, 95% CI: 1.55–4.74, P=0.001) and pleural drainage (OR 2.27, 95% CI: 1.63–2.83, P<0.001). Women were also more likely to require post-discharge pericardial drainage (OR 2.82, 95% CI: 1.72–4.62, P<0.001).

Discussion

Sex difference in CIED acute complications has been a controversial topic of investigation over the past decade. In this study, we systematically explored acute CIED complications in-hospital and 90 days post-discharge in Australia and New Zealand. Our key result is that women experience a higher rate of CIED complications than men. Our data not only confirm a significant sex difference exists for overall CIED implantation, but that the difference is consistent across all CIED types, despite different indications and baseline characteristics, for both acute and elective procedures. The significantly higher complication rates experienced by women is primarily driven by approximate doubling of the risk of in-hospital pleural and pericardial drainage, typically used to treat implant-related complications such as pneumothorax, pericardial effusion, or tamponade.

Although previous studies have observed a trend between women sex and increased CIED complication rates, the existing data on sex differences in CIED complications have been predominantly limited to single device type, also finding a trend towards higher rates of complications in women.[6,7,13] To our knowledge, no national-level population study has systematically examined the impact of sex-differences on overall CIED complications. The current study uses population level data including all CIED types, assesses complications separately for each device type, includes both in-hospital and post-discharge complications, and compares outcomes for women and men for individual complications.

Inclusion of the broadest array of device types increases the external validity and applicability of the study findings. The

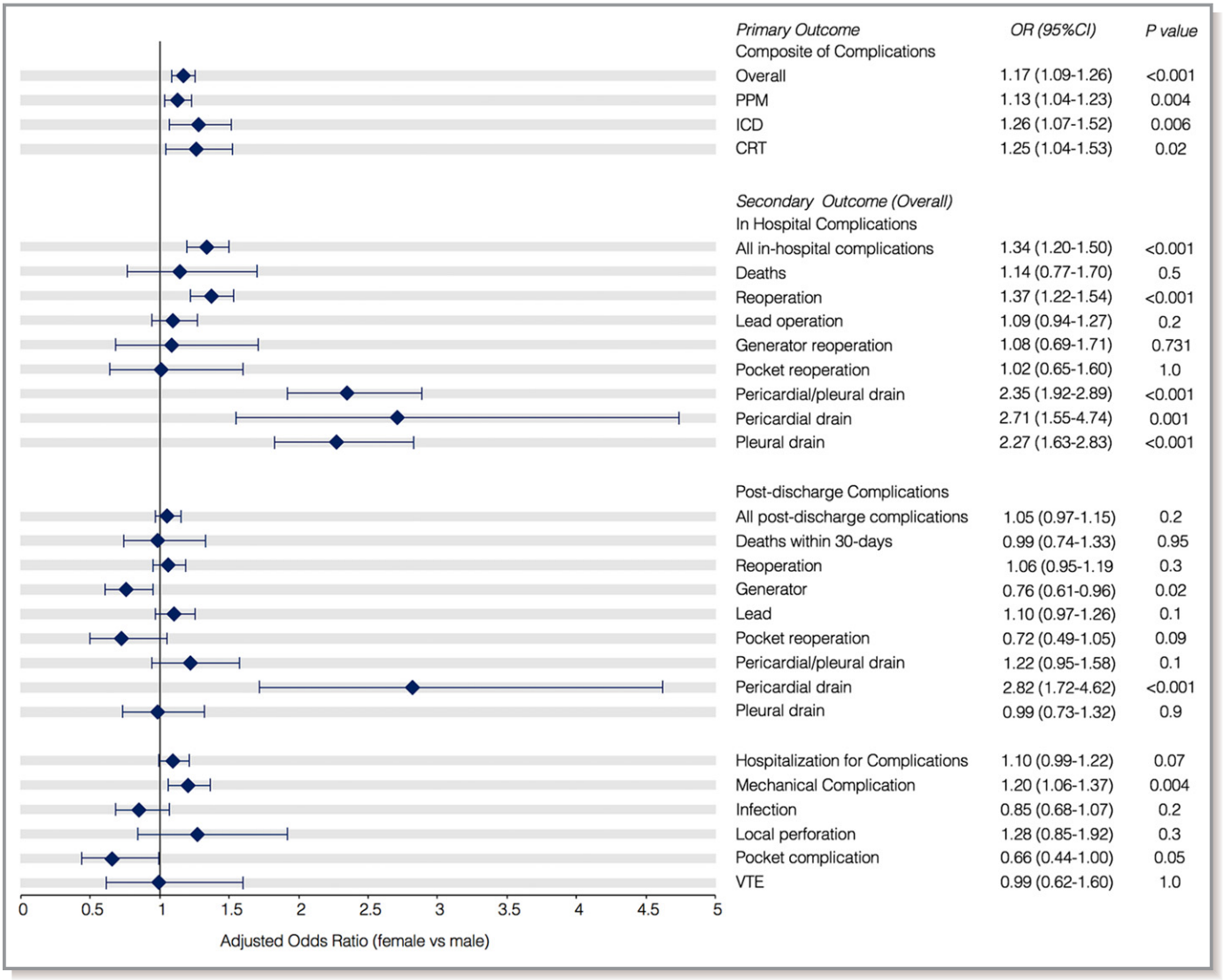

Figure 3. Adjusted risk of elective CIED complications for women vs men overall and by specific complications reported as adjusted odds ratio with 95% CI. CRT indicates cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; OR, odds ratio; PPM, permanent pacemaker; VTE, venous thromboembolism.

excess burden of risk seen in women in both PPM and ICD/CRT suggest that device factors are not responsible for higher rates of complications, but that patient-level differences at implant may be responsible for higher complication rates.

While the exact mechanisms for increase in complications among women remains unclear, we suggest that they can be potentially explained by anatomical differences. Pneumothorax most commonly arises while attempting subclavian vein or axillary vein venipuncture. Our data show that women are twice as likely to require pleural drainage, perhaps explained by sex differences in anatomy, including thinner vessel walls, smaller vessel diameter, and/or less tissue between subclavian vein and pleura. Consistent with these findings, evidence exists to suggest higher rates of complications in women undergoing central venous catheterization.[14]

In our study, women were twice as likely to require in-hospital pericardial drainage because of pericardial effusion or tamponade. Evidence suggests that the myocardial wall is thinner[15,16] and the coronary sinus is smaller[17] in women, perhaps providing a potential mechanism for myocardial perforation.

Implications and Future Directions

The results of the study have significant implications for implantation technique, and potentially the design of new CIED technologies. Firstly, this study highlights the need for increased awareness amongst implanters for higher rates of acute pneumothorax and tamponade among women. Increased education and training of CIED implanters of

the increased risks among women may help to alleviate the disproportionate impact of these complications on women.

Secondly, the results may be important to help drive improvements in technologies. Increased awareness of the discrepancy in endovascular access-related complications may drive increased use of ultrasound, or cephalic access in women to decreased risks of pneumothorax, and perhaps improvements in existing lead technologies to minimize the risk of tamponade.

Study Limitations

The main limitation of this study is that data stem from diagnostic and procedural codes from administrative sources. However, prior studies have shown that accuracy of administrative coding[10] is only modestly lower than that of clinical registries.[18] We have focused on major complications and coding definitions used by prior studies to minimize the risk of erroneous coding. Because of the use of administrative data, patient-level covariates not recorded including body weight and height were not able to be included in the adjustment model.

Only major complications were included as they are more likely to impact patient morbidity and mortality and influence healthcare cost. Minor complications not requiring intervention or readmission were excluded. Additionally, our study was an observational study and there is a possibility of unmeasured confounding. However, analysis of elective procedures in which baseline characteristics are more homogeneous between women and men also showed a consistent increase in complications in women.

Conclusion

Women experience an increased risk of in-hospital and device-related complications within 90 days of first CIED implantation. The sex difference arises primarily through an increased incidence of pleural or pericardial drainage typically used to treat implant-related complications such as pneumothorax, pericardial effusion, or tamponade. Improvements in implant technique and technologies are required to minimize the risk of implant-related complications in women.

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Disclosures

Prof McGavigan has received modest speaker fees and honoraria from Abbott, Biotronik, Boston Scientific, and Medtronic, and has participated in Advisory Boards for Abbott, Boston Scientific, and Medtronic. McGavigan has received fellow and research support from Medtronic. Prof Heddle declares Pfizer speakers bureau and Boehringer Ingelheim. Prof Heddle has received modest honoraria for speaking to General Practitioners about medication (total quantum <$5000 past 5 years) and funds go to a University Trust Fund and is associated with clinical trials with Bristol Myer Squibb and Biotronik. Ms Labrosciano is supported by a Faculty of Health Sciences Divisional Scholarship from the University of Adelaide. Dr Ranasinghe is supported by a National Heart Foundation of Australia Future Leader Fellowship (ID 101186). The remaining authors have no disclosures to report.

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Supplemental Material

Table S1. Procedure codes used to define exclusion criteria.

1) Device replacement

ACHI Procedure Code	Code Description
38353-01	*Replacement of cardiac pacemaker generator*
38393-01	*Replacement of cardiac defibrillator generator*

2) Ablation (open or catheter)

ACHI Procedure Code	Code Description
38287-01	*Catheter ablation of arrhythmia circuit or focus, not elsewhere classified*
38287-02	*Catheter ablation of arrhythmia circuit or focus involving left atrial chamber*
38287-03	*Open ablation of arrhythmia circuit or focus, not elsewhere classified*
38287-04	*Open ablation of arrhythmia circuit or focus involving left atrial chamber*
38290-01	*Catheter ablation of arrhythmia circuit or focus involving both atrial chambers*
38290-02	*Open ablation of arrhythmia circuit or focus involving both atrial chambers*

3) Coronary artery bypass grafting (CABG) or surgery requiring cardio-pulmonary bypass

ACHI Procedure Code	Code Description
38497-00	*Coronary artery bypass, using 1 saphenous vein graft*
38497-01	*Coronary artery bypass, using 2 saphenous vein grafts*
38497-02	*Coronary artery bypass, using 3 saphenous vein grafts*
38497-03	*Coronary artery bypass, using >= 4 saphenous vein grafts*
38497-04	*Coronary artery bypass, using 1 other venous graft*
38497-05	*Coronary artery bypass, using 2 other venous grafts*
38497-06	*Coronary artery bypass, using 3 other venous grafts*
38497-07	*Coronary artery bypass, using >= 4 other venous grafts*
38500-00	*Coronary artery bypass, using 1 LIMA graft*
38503-00	*Coronary artery bypass, using >= 2 LIMA grafts*
38500-01	*Coronary artery bypass, using 1 RIMA graft*
38503-01	*Coronary artery bypass, using >= 2 RIMA grafts*
38500-02	*Coronary artery bypass, using 1 radial artery graft*
38503-02	*Coronary artery bypass, using >= 2 radial artery grafts*
38500-03	*Coronary artery bypass, using 1 epigastric artery graft*
38503-03	*Coronary artery bypass, using >= 2 epigastric artery grafts*

38500-04	*Coronary artery bypass, using 1 other arterial graft*
38503-04	*Coronary artery bypass, using >= 2 other arterial grafts*
38500-05	*Coronary artery bypass, using 1 composite graft*
38503-05	*Coronary artery bypass, using >= 2 composite grafts*
90201-00	*Coronary artery bypass, using 1 other graft, not elsewhere classified*
90201-01	*Coronary artery bypass, using 2 other grafts, not elsewhere classified*
90201-02	*Coronary artery bypass, using 3 other grafts, not elsewhere classified*
90201-03	*Coronary artery bypass, using >= 4 other grafts, not elsewhere classified*

Table S2. Procedure codes used to identify generator, lead or pocket reoperation.

Reoperation Type	Group	Code	Code Description
Generator	Removal	*38353-02*	*Removal of cardiac pacemaker generator*
		90203-07	*Removal of cardiac defibrillator generator*
	Revision	*90203-05*	*Adjustment of cardiac pacemaker generator*
		90203-06	*Adjustment of cardiac defibrillator generator*
	Replacement	*38353-01*	*Replacement of cardiac pacemaker generator*
		38393-01	*Replacement of cardiac defibrillator generator*
Lead	Insertion	*38350-00*	*Insertion of permanent transvenous electrode into other heart chamber(s) for cardiac pacemaker*
		38368-00	*Insertion of permanent transvenous electrode into left ventricle for cardiac pacemaker*
		38390-01	*Insertion of permanent transvenous electrode into left ventricle for cardiac defibrillator*
		38390-02	*Insertion of permanent transvenous electrode into other heart chamber(s) for cardiac defibrillator*
	Removal	*38350-02*	*Removal of permanent transvenous electrode of other heart chamber(s) for cardiac pacemaker*
		38350-04	*Removal of permanent transvenous electrode of other heart chamber(s) for cardiac defibrillator*
		38358-00	*Removal of permanent transvenous electrode of other heart chamber(s) for cardiac pacemaker using extraction device*
		38358-01	*Removal of permanent transvenous electrode of left ventricle for cardiac pacemaker using extraction device*
		38358-02	*Removal of permanent transvenous electrode of left ventricle for cardiac defibrillator using extraction device*
		38358-03	*Removal of permanent transvenous electrode of other heart chamber(s) for cardiac defibrillator using extraction device*
		38368-02	*Removal of permanent transvenous electrode of left ventricle for cardiac pacemaker*
		38368-04	*Removal of permanent transvenous electrode of left ventricle for cardiac defibrillator*
		38456-26	*Removal of permanent epicardial electrode for cardiac pacemaker via subxyphoid approach*
		38456-27	*Removal of permanent epicardial electrode for cardiac pacemaker via thoracotomy or sternotomy*
		38456-33	*Removal of permanent epicardial electrode for cardiac defibrillator via subxyphoid approach*

	38456-34	*Removal of permanent epicardial electrode for cardiac defibrillator via thoracotomy or sternotomy*
	38654-02	*Removal of permanent left ventricular electrode for cardiac pacemaker via thoracotomy or sternotomy*
	38654-05	*Removal of permanent left ventricular electrode for cardiac defibrillator via thoracotomy or sternotomy*
	38350-02	*Removal of permanent transvenous electrode of other heart chamber(s) for cardiac pacemaker*
	38350-04	*Removal of permanent transvenous electrode of other heart chamber(s) for cardiac defibrillator*
	38358-00	*Removal of permanent transvenous electrode of other heart chamber(s) for cardiac pacemaker using extraction device*
	38358-01	*Removal of permanent transvenous electrode of left ventricle for cardiac pacemaker using extraction device*
	38358-02	*Removal of permanent transvenous electrode of left ventricle for cardiac defibrillator using extraction device*
Replacement	*38350-01*	*Replacement of permanent transvenous electrode of other heart chamber(s) for cardiac pacemaker*
	38350-03	*Replacement of permanent transvenous electrode of other heart chamber(s) for cardiac defibrillator*
	38368-01	*Replacement of permanent transvenous electrode of left ventricle for cardiac pacemaker*
	38368-03	*Replacement of permanent transvenous electrode of left ventricle for cardiac defibrillator*
	38456-23	*Replacement of permanent epicardial electrode for cardiac pacemaker via subxyphoid approach*
	38456-24	*Replacement of permanent epicardial electrode for cardiac pacemaker via thoracotomy or sternotomy*
	38456-30	*Replacement of permanent epicardial electrode for cardiac defibrillator via subxyphoid approach*
	38456-31	*Replacement of permanent epicardial electrode for cardiac defibrillator via thoracotomy or sternotomy*
	38654-01	*Replacement of permanent left ventricular electrode for cardiac pacemaker via thoracotomy or sternotomy*
	38654-04	*Replacement of permanent left ventricular electrode for cardiac defibrillator via thoracotomy or sternotomy*
	38350-01	*Replacement of permanent transvenous electrode of other heart chamber(s) for cardiac pacemaker*
	38350-03	*Replacement of permanent transvenous electrode of other heart chamber(s) for cardiac defibrillator*
	38368-01	*Replacement of permanent transvenous electrode of left ventricle for cardiac pacemaker*

	38368-03	*Replacement of permanent transvenous electrode of left ventricle for cardiac defibrillator*
	38456-23	*Replacement of permanent epicardial electrode for cardiac pacemaker via subxyphoid approach*
	38456-24	*Replacement of permanent epicardial electrode for cardiac pacemaker via thoracotomy or sternotomy*
Revision	*38456-21*	*Adjustment of epicardial electrode for cardiac pacemaker*
	38456-28	*Adjustment of epicardial electrode for cardiac defibrillator*
	90203-00	*Adjustment of transvenous electrode for cardiac pacemaker*
	90203-02	*Adjustment of left ventricular electrode for cardiac pacemaker via thoracotomy, sternotomy or subxyphoid approach*
	90203-08	*Adjustment of transvenous electrode for cardiac defibrillator*
	90203-09	*Adjustment of left ventricular electrode for cardiac defibrillator via thoracotomy, sternotomy or subxyphoid approach*
	38456-21	*Adjustment of epicardial electrode for cardiac pacemaker*
	38456-28	*Adjustment of epicardial electrode for cardiac defibrillator*
	90203-00	*Adjustment of transvenous electrode for cardiac pacemaker*
	90203-02	*Adjustment of left ventricular electrode for cardiac pacemaker via thoracotomy, sternotomy or subxyphoid approach*
	90203-08	*Adjustment of transvenous electrode for cardiac defibrillator*
	90203-09	*Adjustment of left ventricular electrode for cardiac defibrillator via thoracotomy, sternotomy or subxyphoid approach*
Insertion (Surgical)	*38470-00*	*Insertion of permanent epicardial electrode for cardiac pacemaker via thoracotomy or sternotomy*
	38470-01	*Insertion of permanent epicardial electrode for cardiac defibrillator via thoracotomy or sternotomy*
	38473-00	*Insertion of permanent epicardial electrode for cardiac pacemaker via subxyphoid approach*
	38473-01	*Insertion of permanent epicardial electrode for cardiac defibrillator via subxyphoid approach*
	38654-00	*Insertion of permanent left ventricular electrode for cardiac pacemaker via thoracotomy or sternotomy*
	38654-03	*Insertion of permanent left ventricular electrode for cardiac defibrillator via thoracotomy or sternotomy*

Pocket	Revision	*90219-00*	*Revision or relocation of skin pocket for cardiac pacemaker or defibrillator*

Table S3. Diagnoses and procedure codes used to identify in-hospital device-related complications.

Complication	Code	Description
Infective endocarditis	*I33*	*Acute and subacute endocarditis*
	I33.0	*Acute and subacute infective endocarditis*
	I33.9	*Acute endocarditis, unspecified*
	I38	*Endocarditis, valve unspecified*
Post-procedural shock	*T81.1*	*Postprocedural shock*
Pericardial/Pleural drainage	*38359-00*	*Pericardiocentesis*
	38450-00	*Transthoracic drainage of pericardium*
	38450-01	*Thoracoscopic drainage of pericardium*
	38452-00	*Subxyphoid drainage of pericardium*
	38803-00	*Therapeutic thoracocentesis*
	38806-00	*Insertion of intercostal catheter for drainage*
Incision and drainage of haematoma, seroma or abscess	*30223-00*	*Incision and drainage of haematoma of skin and subcutaneous tissue*
	30223-01	*Incision and drainage of abscess of skin and subcutaneous tissue*
	30223-02	*Other incision and drainage of skin and subcutaneous tissue*
	30223-00	*Incision and drainage of haematoma of skin and subcutaneous tissue*

Table S4. Primary diagnoses codes used to identify post-discharge hospitalizations for device-related complications.

Complication	Subtype	Code	Description
Mechanical Complication	Mechanical Complication	*T82.1*	*Mechanical complication of cardiac electronic device*
		T82.5	*Mechanical complication of other cardiac and vascular devices and implants*
		T82.8	*Other specified complications of cardiac and vascular prosthetic devices, implants and grafts*
		T82.9	*Unspecified complication of cardiac and vascular prosthetic device, implant and graft*
Infection	Device specific infection	*T82.7*	*Infection and inflammatory reaction due to other cardiac and vascular devices, implants and grafts*
	Endocarditis	*I33*	*Acute and subacute endocarditis*
		I33.0	*Acute and subacute infective endocarditis*
		I33.9	*Acute endocarditis, unspecified*
		I38	*Endocarditis, valve unspecified*
		I39	*Endocarditis and heart valve disorders in diseases classified elsewhere*
		I40.0	*Infective myocarditis*
		T82.6	*Infection and inflammatory reaction due to cardiac valve prosthesis*
	Other infection complicating the procedure	*T81.42*	*Sepsis following a procedure*
		U90	*Healthcare associated infections*
		U90.0	*Healthcare associated Staphylococcus aureus bacteraemia*
Perforation	Pneumothorax	*J93*	*Pneumothorax*
		J93.2	*Iatrogenic pneumothorax*
		J93.8	*Other pneumothorax*
		J93.9	*Pneumothorax, unspecified*
	Pleural Effusion	*J94.2*	*Haemothorax*
		J86	*Pyothorax*
		J86.0	*Pyothorax with fistula*
		J86.9	*Pyothorax without fistula*
		J90	*Pleural effusion, not elsewhere classified*
		J91	*Pleural effusion in conditions classified elsewhere*
	Hemopericardium	*I31.2*	*Hemopericardium, not elsewhere classified*
	Pericardial Effusion	*I31.3*	*Pericardial effusion (noninflammatory)*

	Perforation	*T81.2*	*Accidental puncture and laceration during a procedure, not elsewhere classified*
Pocket related complications	Haemorrhage or Haematoma	*T81.0*	*Haemorrhage and haematoma complicating a procedure, not elsewhere classified*
	Wound Disruption	*T81.3*	*Disruption of operation wound, not elsewhere classified*
		T81.4	*Wound infection following a procedure, not elsewhere classified*
		T81.41	*Wound infection following a procedure*
Other	Other procedure related complications	*T81.1*	*Shock during or resulting from a procedure, not elsewhere classified*
		T81.5	*Foreign body accidentally left in body cavity or operation wound following a procedure*
		T81.6	*Acute reaction to foreign substance accidentally left during a procedure*
		T81.7	*Vascular complications following a procedure, not elsewhere classified*
		T81.9	*Unspecified complication of procedure*

Table S5. Adjusted odds ratio of CIED complications for female vs male after covariate adjustment*.

	PPM				ICD				CRT				Overall			
	OR	**5th**	**95th**	**P**	**OR**	**5th**	**95th**	**P**	**OR**	**5th**	**95th**	**P**	**OR**	**5th**	**95th**	**P**
Primary Outcome Composite of Early device-related Complications	1.06	1.00	1.13	0.061	1.25	1.09	1.44	0.002	1.22	1.04	1.43	0.013	1.10	1.04	1.16	<0.001
In-Hospital Complications																
All complications	1.16	1.06	1.27	0.001	1.41	1.11	1.77	0.004	1.31	1.03	1.67	0.027	1.20	1.11	1.30	<0.001
Death	0.98	0.79	1.22	0.860	1.85	0.62	5.49	0.268	0.67	0.26	1.74	0.408	0.99	0.80	1.22	0.897
Reoperation	1.19	1.08	1.31	<0.001	1.39	1.10	1.77	0.006	1.41	1.10	1.81	0.007	1.23	1.13	1.34	<0.001
o Lead operation	0.98	0.86	1.12	0.779	1.03	0.74	1.43	0.865	1.19	0.86	1.64	0.307	1.01	0.90	1.13	0.843
o Generator	0.97	0.65	1.44	0.859	1.41	0.50	3.99	0.519	0.79	0.31	2.02	0.615	0.97	0.69	1.37	0.864
o Pocket reoperation	0.90	0.60	1.34	0.597	0.86	0.37	1.99	0.718	0.95	0.38	2.35	0.909	0.91	0.65	1.27	0.568
o Pericardial/pleural drain	1.81	1.54	2.14	<0.001	2.34	1.58	3.47	<0.001	2.31	1.49	3.60	<0.001	1.91	1.65	2.21	<0.001
• Pericardial drain	2.01	1.31	3.08	0.001			-				-		2.17	1.48	3.18	<0.001
• Pleural drain	1.78	1.49	2.12	<0.001	2.12	1.39	3.23	0.001	2.29	1.44	3.64	0.001	1.86	1.59	2.17	<0.001
Other			-				-				-		1.14	0.65	2.00	0.638
Post-discharge Complications																
All complications	0.97	0.90	1.05	0.511	1.17	0.99	1.38	0.066	1.13	0.93	1.36	0.228	1.02	0.95	1.09	0.603
Death within 30 days	0.91	0.75	1.10	0.347	1.94	1.07	3.51	0.029	1.24	0.72	2.12	0.441	1.00	0.84	1.18	0.951
Reoperation	1.01	0.90	1.12	0.933	1.10	0.89	1.37	0.383	1.14	0.89	1.45	0.307	1.04	0.95	1.13	0.454
o Generator	0.78	0.62	0.97	0.023	1.04	0.71	1.54	0.828	0.80	0.49	1.30	0.367	0.83	0.69	0.99	0.036
o Lead	1.01	0.88	1.14	0.943	1.20	0.94	1.54	0.147	1.23	0.93	1.63	0.152	1.07	0.96	1.19	0.236
o Pocket reoperation	0.72	0.50	1.04	0.079	0.71	0.35	1.45	0.348	0.54	0.24	1.26	0.155	0.69	0.51	0.94	0.018
o Pericardial/pleural drain	1.06	0.85	1.32	0.615	1.29	0.76	2.20	0.346	1.91	1.05	3.46	0.033	1.15	0.95	1.40	0.157
• Pericardial drain	1.99	1.25	3.19	0.004			-				-		2.04	1.38	3.02	0.000
• Pleural drain	0.94	0.73	1.20	0.609	0.93	0.49	1.77	0.829	2.05	1.03	4.10	0.043	1.01	0.81	1.26	0.934
Hospitalization for Complications	1.03	0.94	1.13	0.569	1.13	0.94	1.37	0.205	1.05	0.83	1.32	0.698	1.05	0.97	1.13	0.272
o Mechanical Complication	1.12	0.99	1.27	0.066	1.11	0.87	1.40	0.408	1.10	0.84	1.46	0.483	1.11	1.01	1.23	0.037

o Infection	0.77	0.63	0.95	0.016	1.27	0.86	1.88	0.235	0.80	0.47	1.34	0.389	0.85	0.71	1.01	0.067
o Local perforation~	1.10	0.78	1.54	0.597	0.89	0.33	2.41	0.824	-				1.19	0.88	1.61	0.270
o Pocket complication#	0.76	0.54	1.06	0.109	0.66	0.29	1.48	0.310	0.50	0.20	1.22	0.125	0.71	0.53	0.96	0.024
o VTE	1.24	0.85	1.80	0.269	1.04	0.44	2.42	0.933	-				1.24	0.89	1.73	0.197

*Reported as odds ratios with 95% confidence interval and p-values.

†Infection includes device infection, endocarditis or systemic infection.

‡Local perforation includes perforation and or inflammation such as a pneumothorax or a pericardial effusion.

§Pocket complication includes hematoma or wound dehiscence.

VTE = venous thromboembolism.

OR could not be calculated for individual CIED type for all complications due to low event rate.