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Gender Differences in Procedure-Related Adverse Events in Patients Receiving Implantable Cardioverter-Defibrillator Therapy

Pamela N. Peterson, MD, MSPH; Stacie L. Daugherty, MD, MSPH; Yongfei Wang, MS; Humberto J. Vidaillet, MD; Paul A. Heidenreich, MD; Jephtha P. Curtis, MD; Frederick A. Masoudi, MD, MSPH; on behalf of the National Cardiovascular Data Registry

Background—Women are at higher risk than men for adverse events with certain invasive cardiac procedures. Our objective was to compare rates of in-hospital adverse events in men and women receiving implantable cardioverter-defibrillator (ICD) therapy in community practice.

Methods and Results—Using the National Cardiovascular Data Registry ICD Registry, we identified patients undergoing first-time ICD implantation between January 2006 and December 2007. Outcomes included in-hospital adverse events after ICD implantation. Multivariable analysis assessed the association between gender and in-hospital adverse events, with adjustment for demographic, clinical, procedural, physician, and hospital characteristics. Of 161 470 patients, 73% were male, and 27% were female. Women were more likely to have a history of heart failure (81% versus 77%, $P<0.01$), worse New York Heart Association functional status (57% versus 50% in class III and IV, $P<0.01$), and nonischemic cardiomyopathy (44% versus 27%, $P<0.01$) and were more likely to receive biventricular ICDs (39% versus 34%, $P<0.01$). In unadjusted analyses, women were more likely to experience any adverse event (4.4% versus 3.3%, $P<0.001$) and major adverse events (2.0% versus 1.1%, $P<0.001$). In multivariable models, women had a significantly higher risk of any adverse event (OR 1.32, 95% CI 1.24 to 1.39) and major adverse events (OR 1.71, 95% CI 1.57 to 1.86).

Conclusions—Women are more likely than men to have in-hospital adverse events related to ICD implantation. Efforts are needed to understand the reasons for higher ICD implantation-related adverse event rates in women and to develop strategies to reduce the risk of these events. (*Circulation*. 2009;119:1078-1084.)

Key Words: registries ■ electrophysiology ■ morbidity ■ women

Randomized clinical trials have demonstrated the efficacy of implantable cardioverter-defibrillators (ICDs) in reducing mortality in patients at risk for life-threatening cardiac arrhythmias¹⁻⁵; however, ICD implantation may be associated with adverse events that may attenuate the benefits derived from therapy. With the dramatic increase in the number of ICD implantations,⁶ it is important to understand complications related to implantation. Data regarding implantation-related adverse events from rhythm-management devices, both pacemakers⁷⁻¹¹ and ICDs,¹²⁻¹⁵ are limited because they are derived from clinical trials, single-center reports, or studies using administrative data. Clinical trials of procedures generally include experienced centers and highly selected patient populations.¹⁶⁻¹⁸ Single-center reports also may not reflect the patient populations, practice patterns,

or outcomes in wider community practice. Finally, administrative data are limited with respect to important potential confounders and do not permit standardized definitions of adverse events.

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Studies of some invasive cardiovascular procedures indicate that women are at particularly high risk for procedural complications compared with men. For example, women have higher rates of bleeding, stroke, and in-hospital mortality after revascularization procedures.¹⁹ Proposed explanations are that women are older and have a higher prevalence of comorbidities and risk factors. However, remarkably little is known about gender differences in complications after ICD

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implantation. Although 1 study has reported that women may be more likely to experience ICD implantation–related complications,¹⁴ that study was confined to the Medicare population and was limited to administrative data to characterize the study population and to identify complications.

Accordingly, we hypothesized that women would be more likely than men to experience an implantation-related adverse event after ICD implantation. To address this question, we used data from a national registry that contained detailed clinical data and used standardized definitions of adverse events for patients undergoing ICD implantation in community practice. We studied ICD implantation–related adverse event rates among men and women and evaluated whether complication rates varied according to important patient and device factors.

Methods

Data Source

Analyses used data from the National Cardiovascular Data Registry ICD Registry. In January 2005, in conjunction with the expansion of coverage for ICDs used for primary prevention, the Center for Medicare and Medicaid Services mandated that hospitals participate in a national ICD registry. Because many questions about the safety and effectiveness of primary prevention ICDs remain, the Center for Medicare and Medicaid Services used the expansion of coverage to support the development of an ICD registry to gather additional practical evidence to help clinicians and patients make informed decisions.²⁰ Although the Center for Medicare and Medicaid Services mandate requires only that Medicare patients receiving primary prevention ICDs be entered into the database, secondary prevention implantations are also represented, because the majority of hospitals voluntarily enter information on all ICD implantations regardless of indication or insurance status.²¹ Clinical, demographic, and procedural information is collected in addition to information about adverse events until the time of discharge by use of standardized data elements and definitions. Data are submitted by participating hospitals using American College of Cardiology–certified software, and data quality is examined with the Data Quality Reporting process.²¹ Implanting centers must enter complete and accurate data to receive Medicare reimbursement.

Study Population

Between January 2006 and December 2007, 1224 hospitals submitted data to the National Cardiovascular Data Registry ICD Registry that passed the Data Quality Reporting thresholds. Data included 204 700 unique patients undergoing device implantation. We identified a final cohort of 161 470 patients undergoing first-time ICD implantation, excluding patients who had undergone a prior ICD implantation (n=43 230).

Outcomes

The occurrence of any adverse event during the hospitalization for ICD implantation was the primary end point, and the occurrence of major adverse events was the secondary end point. Events that occur during or after the implantation procedure until the time of hospital discharge are reported by implanting centers using standard definitions as outlined in the Appendix (Data Supplement). Major adverse events included cardiac arrest, cardiac perforation, cardiac valve injury, coronary venous dissection, hemothorax, pneumothorax, deep phlebitis, transient ischemic attack, stroke, myocardial infarction, pericardial tamponade, and arteriovenous fistula. *Any adverse event* included both major adverse events as described above and drug reaction, conduction block, hematoma, lead dislodgment, peripheral embolus, superficial phlebitis, peripheral nerve injury, and infection related to the device. In secondary analyses, hospital length of stay (in days) was assessed.

Predictor Variable and Confounding Variables

The primary predictor variable of interest was patient gender. The other confounding variables considered were patient demographics (age, race, insurance payer); reason for hospitalization; patient comorbidities and risk factors (history of congestive heart failure, atrial fibrillation or flutter, cardiac transplantation, cause of cardiomyopathy, myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, valvular surgery, cerebrovascular disease, pacemaker insertion, chronic lung disease, diabetes mellitus, hypertension, renal failure [hemodialysis], and admission New York Heart Association classification); diagnostic information (ejection fraction, whether an electrophysiology study was performed, electrophysiology study results, QRS duration, PR interval, presence of atrial or ventricular conduction delays, creatinine, serum urea nitrogen, sodium level, brain natriuretic peptide level, and systolic blood pressure); procedural information (ICD type [single-chamber, dual-chamber, or biventricular ICD] and lead implantation method); and physician and hospital characteristics (whether the implanting physician is certified in electrophysiology per self-report, for-profit or not-for-profit hospital, rural or nonrural hospital, hospital teaching status, number of beds, and annual number of ICD implantations at each hospital).

The rate of missing data was extremely low for all variables (<0.5%, with the exception of left ventricular ejection fraction, which was missing in 1.5% of cases). To avoid casewise deletion of those cases with missing data points, the missing values were imputed. For categorical variables, the missing variables were imputed as the most common value among those with the data present. For example, for the categorical variable of New York Heart Association class, which was missing in 0.15% of cases, missing values were imputed as class I. For continuous variables, the missing values were imputed as the median among those with the data present. Dummy variables were constructed to indicate when the variable was missing. In the multivariable models, both the imputed values and the dummy variable were included.

Statistical Analysis

Baseline demographic and clinical factors were compared between men and women with the χ^2 test for categorical variables and *t* tests for continuous variables. The rates of in-hospital adverse events were compared between men and women with the χ^2 test.

The independent association of gender with device implantation–related adverse events was assessed with hierarchical logistic regression with PROC GLIMMIX, with accounting for clustering of patients within hospitals. The demographic, clinical, procedural, and physician characteristics in Table 1 were all included in the models. The single physician-level characteristic was treated as a patient-level factor. No variable selection procedures were performed.

The relationship between gender and adverse events was also explored in prespecified subgroups. Because older people are more prone to adverse events from invasive procedures, and because biventricular ICD implantation is a more extensive and time-consuming procedure, analyses were stratified by age and device type. Additionally, patients were stratified by payer and indication (primary versus secondary prevention). Multivariable hierarchical logistic regression models were constructed by use of the same approach as the full risk models, stratified by each of the prespecified subgroups. The statistical significance of differences among strata was tested with 2-way interaction terms in full models.

In the secondary multivariable analyses of length of stay, the outcome was log-transformed to accommodate the skewed distribution of this variable. After regression, the adjusted length of stay was exp-transformed back to its natural unit. All analyses were performed with the SAS statistical package version 9.1 (SAS Institute, Cary, NC).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Table 1. Baseline Characteristics of Men and Women

Variable	Men (n=117 815)	Women (n=43 655)	P
Demographics			
Age: mean (SD), y	67.9 (12.6)	67.0 (13.6)	<0.0001
Race, %			<0.001
White	83.7	77.4	
Black	10.9	17.5	
Other	5.3	5.1	
Hispanic	5.2	5.2	0.760
Insurance, %			<0.001
Medicare	67.3	66.9	
Medicaid	4.0	6.1	
Commercial	18.0	17.0	
HMO	6.8	6.5	
Other	4.1	3.5	
Reason for hospitalization, %			<0.001
For ICD procedure	62.0	60.0	
Cardiac	12.3	14.3	
Noncardiac	22.6	22.0	
Unknown	3.1	3.4	
Cardiac history and risk factors			
Indication: primary prevention, %	72.0	72.2	0.531
Sustained VT, %	11.0	10.1	<0.001
Syncope, %	18.8	19.8	<0.001
History of heart failure, %	76.8	81.0	<0.001
Ejection fraction, mean (SD), %	27.1 (10.2)	27.6 (11.6)	<0.001
NYHA class at time of procedure, %			<0.001
Class I	12.9	11.2	
Class II	36.9	31.6	
Class III	45.7	52.0	
Class IV	4.4	5.2	
Atrial fibrillation/flutter, %	32.9	26.7	<0.001
Nonischemic dilated cardiomyopathy, %	27.2	44.3	<0.001
Ischemic heart disease, %	71.1	50.6	<0.001
Previous MI, %	58.9	41.0	<0.001
Previous CABG, %	39.3	21.5	<0.001
Previous PCI, %	34.6	25.8	<0.001
Previous valvular surgery, %	7.1	8.1	<0.001
Additional medical history, %			
Cerebrovascular disease	14.9	13.8	<0.001

(Continued)

Table 1. Continued

Variable	Men (n=117 815)	Women (n=43 655)	P
Chronic lung disease	22.2	23.0	<0.001
Diabetes mellitus	36.6	37.9	<0.001
Hypertension	74.8	73.1	<0.001
Renal failure–dialysis	4.2	4.1	0.714
Procedure characteristics			
Electrophysiology study done, %	15.5	12.7	<0.001
QRS duration, mean (SD), ms	126 (34)	125 (35)	<0.001
ICD type, %			<0.001
Single chamber	24.9	23.5	
Dual chamber	40.9	37.2	
Biventricular	34.1	39.1	
Laboratory data			
Creatinine, mean (SD), mg/dL	1.44 (1.17)	1.27 (1.08)	<0.001
Sodium, mean (SD), mEq/L	138 (3.5)	139 (3.5)	0.001
BNP, mean (SD), pg/mL	967 (1099)	1073 (1178)	<0.001
Physician characteristics			
Physician certified in electrophysiology, %			0.382
Yes	62.8	63.1	
No	10.5	10.5	
Unknown	26.7	26.4	
Hospital characteristics			
Private/community, %	85.9	85.5	0.043
Rural, %	10.2	9.9	0.181
Patient beds >450, %	48.6	49.3	0.014
Teaching hospital, %	54.4	54.7	0.305
No. of ICD implantations >220 per year	43.1	43.7	0.029

HMO indicates health maintenance organization; VT, ventricular tachycardia; NYHA, New York Heart Association; MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; and BNP, brain natriuretic peptide.

Results

Of the 161 470 patients, 73% were men, and 27% were women. Women were more likely to have a history of heart failure, worse New York Heart Association functional status, and nonischemic cardiomyopathy. Women were also more likely to receive biventricular ICDs (Table 1). Given the large number of patients in the present study cohort, differences in baseline characteristics may be statistically significant but have little clinical significance.

The overall rate of any adverse event in the entire cohort was 3.6%, with a higher rate in women than in men (4.4% versus 3.3%, $P<0.001$; Figure 1). The rate of major adverse

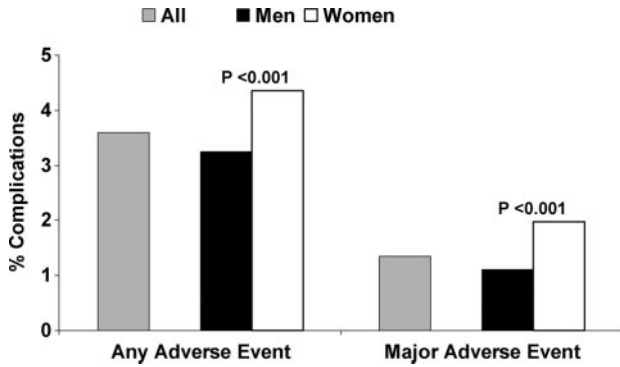


Figure 1. Rates of any adverse event and major adverse events in the total population, men and women.

events in women was nearly double that of men (2.0% versus 1.1%, $P < 0.001$), with an overall rate of 1.3% (Figure 1). When adverse events were considered individually, hematoma and lead dislodgment were the most common. Women were more likely to have a drug reaction, cardiac perforation, conduction block, coronary venous dissection, lead dislodgment, hemothorax, pneumothorax, deep phlebitis, and pericardial tamponade (Table 2). The rates of cardiac arrest, valve

injury, hematoma, peripheral nerve injury, peripheral embolus, superficial phlebitis, transient ischemic attack or stroke, myocardial infarction, arteriovenous fistula, and infection did not differ significantly between men and women (Table 2). In-hospital mortality, which was not considered among adverse events, was not different between men and women (Table 2).

Hospital length of stay was longer among all patients with a reported complication (7.11 days) than among those without a complication (3.83 days, $P < 0.001$). The difference in length of stay was significant across strata according to the reason for admission, including those who were admitted specifically for the ICD implantation ($n = 99\ 250$). In this group, length of stay was significantly higher in patients with a complication (3.91 days) than in those without a complication (1.50 days, $P < 0.0001$). In adjusted analyses, length of stay was significantly higher in patients with complications, by 11.3 days ($P < 0.0001$).

After adjustment for demographic, admission, clinical, and physician factors, women had significantly higher odds of any adverse event (OR 1.32, 95% CI 1.24 to 1.39) and major adverse events (OR 1.71, 95% CI 1.57 to 1.86) than men. Additionally, in stratified analyses, the gender difference in

Table 2. Adverse Event Rates for Total Population and by Gender

	All (n=161 470)	Men (n=117 815)	Women (n=43 655)	P
Major adverse events				
Pneumothorax	822 (0.51)	442 (0.38)	380 (0.87)	<0.001
Cardiac arrest	555 (0.34)	419 (0.36)	136 (0.31)	0.179
Coronary venous dissection	239 (0.15)	133 (0.11)	106 (0.24)	<0.001
Hemothorax	155 (0.10)	91 (0.08)	64 (0.15)	<0.001
Pericardial tamponade	149 (0.09)	66 (0.06)	83 (0.19)	<0.001
Cardiac perforation	136 (0.08)	56 (0.05)	80 (0.18)	<0.001
Stroke	106 (0.07)	76 (0.06)	30 (0.07)	0.769
Myocardial infarction	53 (0.03)	36 (0.03)	17 (0.04)	0.409
Infection related to device	53 (0.03)	38 (0.03)	15 (0.03)	0.836
Deep phlebitis	42 (0.03)	23 (0.02)	19 (0.04)	0.008
TIA	35 (0.02)	26 (0.02)	9 (0.02)	0.860
AV fistula	11 (0.01)	6 (0.01)	5 (0.01)	0.169
Cardiac valve injury	3 (0.00)	3 (0.00)	0 (0.00)	0.292
Total patients with major adverse events	2175 (1.35)	1311 (1.11)	864 (1.98)	<0.001
Minor adverse events				
Hematoma	1719 (1.06)	1258 (1.07)	461 (1.06)	0.838
Lead dislodgment	1767 (1.09)	1231 (1.04)	536 (1.23)	0.002
Drug reaction	170 (0.11)	110 (0.09)	60 (0.14)	0.015
Superficial phlebitis	75 (0.05)	50 (0.04)	25 (0.06)	0.219
Conduction block	70 (0.04)	38 (0.03)	32 (0.07)	<0.001
Peripheral embolus	55 (0.03)	32 (0.03)	23 (0.05)	0.014
Peripheral nerve injury	8 (0.00)	5 (0.00)	3 (0.01)	0.505
Total patients with minor adverse events	3740 (2.32)	2639 (2.24)	1101 (2.52)	<0.001
Total patients with adverse events (major or minor)	5734 (3.55)	3832 (3.25)	1902 (4.36)	<0.001
In-hospital mortality	678 (0.42)	487 (0.41)	191 (0.44)	0.505

TIA indicates transient ischemic attack; AV, arteriovenous. Values are n (%).

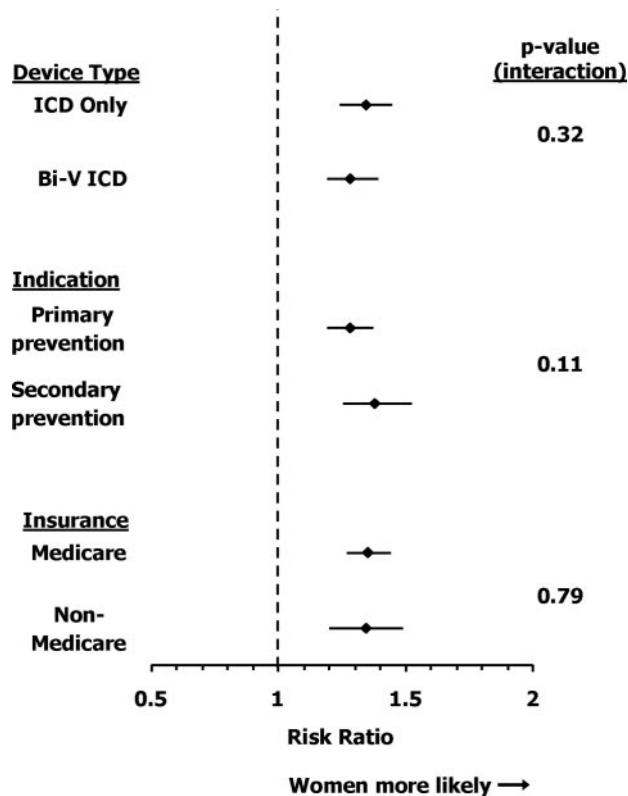


Figure 2. Relationship between gender and any adverse event in subgroups. Bi-V ICD indicates biventricular ICD.

rate of any adverse event was greater among patients ≥ 65 years (OR 1.38, 95% CI 1.29 to 1.48) than in those < 65 years (OR 1.18, 95% CI 1.07 to 1.31; P for age-gender interaction=0.023). However, the association between gender and any adverse event did not vary by device type or indication for implantation (Figure 2). Similarly, the association between gender and major adverse events did not vary within any of the predefined subgroups.

Discussion

Among patients receiving ICDs, women had a higher rate of any adverse event and almost double the rate of major adverse events compared with men. After accounting for demographic, clinical, and procedural differences between men and women, women had 32% higher odds of experiencing an adverse event and 71% higher odds of experiencing a major adverse event than men.

The present study expands the current knowledge of ICD implantation-related adverse events by evaluating a broad range of adverse events in a large cohort of patients receiving ICDs in real-world clinical practice. The observed adverse event rate of 3.6% is consistent with clinical trial data in which adverse event rates range from 1.3% to 5% for ICD implantation.^{1,4,22,23} Of note, clinical trials have not consistently defined or reported adverse events, which renders comparisons among these studies difficult. The present findings are also consistent with the short-term adverse event rate of 3.2% found among a nationwide sample of > 900 hospitals for device implantations from 1997 to 2004.⁶ The adverse event rate we observed is lower than the 10.8% rate previ-

ously reported among Medicare beneficiaries receiving ICDs; however, that study was limited by the use of administrative data to identify adverse events, inclusion of both initial and replacement implantations, evaluation of Medicare beneficiaries only, lack of contemporary data, and low hospital implantation volume.¹⁴ Finally, the present findings are consistent with the perioperative complication rate of 3.7% observed in the Ontario ICD Database.²⁴ This database is comparable to the US National Cardiovascular Data Registry ICD Registry in that it is a prospective registry of patients undergoing ICD implantation with mandated participation by the Ministry of Health and Long-Term Care in Ontario. Trained data collectors enter data into the Ontario ICD Database, and quality controls include random site audits with reabstraction of randomly selected charts by central study personnel.

The most important contribution of the present study is the comparison of gender-specific ICD implantation-related adverse event rates. The association between female gender and adverse outcomes found in the present study is consistent with previous studies that examined this relationship for percutaneous coronary intervention and coronary artery bypass grafting.¹⁹ Postulated reasons for the higher complication rates observed with these revascularization procedures are that women with cardiovascular disease are older and have a higher prevalence of comorbidities and risk factors such as diabetes mellitus, peripheral vascular disease, and hypertension.¹⁹ In the large cohort of patients we studied, men and women did not differ with respect to age, and although women did have a higher prevalence of comorbidities and risk factors, after adjustment for these factors, the association between sex and adverse events persisted. Thus, the factors thought to contribute to higher complication rates in women after other procedures do not appear to entirely explain the higher adverse event rate observed with ICD implantation.

Smaller body size is another proposed explanation for the differences in outcomes seen with revascularization procedures and may explain the higher adverse event rate observed in women with ICD device implantation. Indeed, many of the adverse events that were more common in women were mechanical (cardiac perforation, coronary venous dissection, lead dislodgment, hemothorax, pneumothorax, and pericardial tamponade). This suggests that women may have anatomy that poses greater technical challenges, such as a thinner right ventricular wall and smaller blood vessel diameter, which may predispose them to adverse events. Because neither body mass index or body surface area was available in the National Cardiovascular Data Registry data set, the extent to which variations in body size attenuate gender differences in complication rates could not be ascertained. The present findings are consistent with the few existing studies of pacemaker implantation-associated adverse events that found mechanical complications including lead dislodgment and pneumothorax to be most common.⁷⁻¹¹ However, gender has not been identified as a risk factor for pacemaker-related adverse events. Studies of adverse events associated with pacemaker implantation are limited because they were single-

center reports, used small cohorts, or were performed in clinical trial cohorts.

The reasons for higher adverse event rates in women with ICD implantation should be investigated and, where possible, eliminated. Improvements have occurred over time in the outcomes of women undergoing revascularization with percutaneous coronary intervention and coronary artery bypass grafting.^{25–27} Improvements in outcomes may be due to improved patient selection, advances in technology and procedural techniques, greater operator experience, and refinement of perioperative management and adjunctive medical therapy. Future studies are needed to investigate the reasons for differences in ICD implantation–related adverse event rates between men and women so that measures can be taken to reduce the increased risk in women.

The findings of the present study should not be interpreted to suggest that practitioners should use different thresholds to implant ICDs in women than in men. The decision to pursue this therapy should be based primarily on estimates of the mortality benefits of therapy and patient preferences. However, it is plausible that nonfatal adverse events may influence both cost and patient-centered outcomes, such as quality of life after device implantation. Thus, studies to understand the impact of ICD complications on these other outcomes are warranted in parallel with efforts to understand the causes and reduce the incidence of complications.

The results of the present study highlight the important role of registries in the evaluation of adverse events outside the context of clinical trials. The assessment of harm is often inadequate in randomized trials for several reasons. First, randomized trials are generally underpowered to evaluate adverse events. Second, selection criteria in clinical trials may result in populations with different adverse event profiles.^{17,18,28} Third, the sites performing procedures in clinical trials are often limited in number and have clinicians with a greater level of training and experience performing the procedure.^{16,17} Thus, adverse event rates from clinical trials may not be generalizable. Similarly, single-center reports have limited generalizability. For this reason, the Center for Medicare and Medicaid Services established the National Cardiovascular Data Registry ICD Registry to determine whether outcomes of ICD implantation differ in general practice compared with clinical trials.

Certain factors should be considered in the interpretation of the present study. First, adverse event rates are self-reported by hospitals and may be underreported, which could result in spuriously low adverse event rates; however, because it is unlikely that patterns of reporting would vary by patient gender, any underreporting would result in attenuation of the observed relative risk of complications between sexes.²⁹ Second, the present analysis was limited to short-term in-hospital adverse events. Adverse events such as infections, lead malfunctions, or shocks, which do not manifest until after hospital discharge, were not captured. Additionally, the adverse events captured were limited to those available as data elements in the data collection tool. Events such as incessant ventricular fibrillation at implantation, worsening heart failure, and failed biventricular ICD implantation were not included as adverse events, as they were in some clinical

trials^{1,30}; however, a broad range of implantation-related adverse events important to patients were included in the present analysis. Third, some adverse events are defined by the registry by their most severe consequences (eg, pneumothorax was defined as air in the thorax sufficient to require a chest tube), and therefore, a number of minor complications may not have been captured; however, standard definitions were used for all adverse events independent of patient gender. Finally, we did not have any data on factors such as height, weight, or body mass index and thus were unable to adjust for the potential confounder of body size. Similarly, we did not have information on the lead types used, which may confound the observed difference in the rate of lead dislodgment between men and women.

In summary, in-hospital adverse events occurred in almost 1 in 25 patients undergoing first-time ICD implantation. Gender was a strong and independent factor associated with adverse events in a large cohort of patients receiving an ICD in clinical practice. Although these results should not preclude women from receiving ICDs, a better perspective of the consequences of adverse events on outcomes such as cost and quality of life would be useful to inform decision making concerning ICD implantation. Furthermore, these data support efforts to understand the reasons for higher ICD implantation–related adverse event rates in women and to develop strategies to reduce this risk.

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Disclosures

Dr Heidenreich serves as a consultant for Boston Scientific. Dr Masoudi has served on advisory boards for Takeda NA, Amgen, and United Healthcare; he has received grant funding from Amgen; he has contracts with the American College of Cardiology and the Oklahoma Foundation for Medical Quality; and he serves as an Associate Editor for *Journal Watch Cardiology*, Massachusetts Medical Society, and for *Circulation: Quality of Care and Outcomes*. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

Women are at higher risk than men for adverse events with some invasive cardiac procedures. Despite the dramatic increase in the number of implantations of implantable cardioverter defibrillators (ICDs), data regarding implantation-related adverse events are limited because they are derived from clinical trials, single-center reports, or studies using administrative data. Using the National Cardiovascular Data Registry ICD Registry, we compared rates of in-hospital adverse events in men and women receiving ICD therapy in community practice between January 2006 and December 2007. Of 161 470 patients, 27% were female. Women had a significantly higher risk of any adverse event (4.4% versus 3.3%, $P < 0.001$; adjusted OR 1.32, 95% CI 1.24 to 1.39) and major adverse events (2.0% versus 1.1%, $P < 0.001$; adjusted OR 1.71, 95% CI 1.57 to 1.86). Many of the adverse events that were more common in women were mechanical (cardiac perforation, coronary venous dissection, lead dislodgment, hemothorax, pneumothorax, and pericardial tamponade). Although these results should not preclude women from receiving ICDs, efforts are needed to understand the reasons for higher ICD implantation-related adverse event rates in women and to develop strategies to reduce the risk of these events.

Supplemental Data

Appendix A – Definitions of Adverse Events ICD Registry™

Cardiac Arrest: Sudden cessation of cardiac activity so that the patient became unresponsive, with no normal breathing and no signs of circulation.

Drug Reaction: Anaphylaxis, rash, etc.

Cardiac Perforation: Migration of pacing or defibrillator lead to epicardial surface, resulting in pain, pericardial effusion, failure to capture, capture of diaphragm, phrenic nerve, or intercostals muscle of sufficient magnitude to require repositioning.

Cardiac Valve Injury: Manipulation of pacing or defibrillating leads that may tear a valve leaflet or chordae tendinae (usually manifests as a new regurgitant murmur appearing after the procedure).

Conduction Block: If the patient experienced a conduction block as documented by manipulation of pacing or defibrillating leads that may injure parts of the specialized cardiac conducting system. (Usually manifest as a new RBBB or new on set of complete heart block in a person with preexisting LBBB).

Coronary Venous Dissection: Manipulation of pacing or defibrillating leads in the coronary sinus (CS) may result in a tear of the CS endothelium, with dissection into the CS wall. This may occasionally result in perforation of the CS.

Hematoma: Hematoma resulting in re-operation or transfusion.

Lead Dislodgement: Movement of lead sufficient to require repositioning.

Hemothorax: As documented by accumulation of blood in thorax.

Pneumothorax: Air in thorax sufficient to require chest tube.

Peripheral Nerve Injury: Sensory or motor loss of peripheral nerve function. This may result from external nerve compression as a result of positioning during an implantation procedure, internal compression (e.g. secondary to hematoma formation) or direct nerve injury.

Peripheral Embolus: Acute occlusion of an artery resulting from embolization of a cardiac or proximal arterial thrombus.

Phlebitis – Superficial: As documented by signs of superficial venous inflammation, such as local erythema, tenderness or swelling.

Phlebitis – Deep: As documented by occlusion of deep vein resulting in extremity swelling, plus or minus signs of inflammation.

TIA: Loss of neurological function that was abrupt in onset but with complete return of function within 24 hours.

CVA/Stroke: A central neurological deficit persisting for > 72 hours.

Pericardial Tamponade: Fluid in the pericardial space compromising cardiac filling, and requiring intervention as documented by either: 1) Echo showing pericardial fluid and signs of tamponade such as right heart compromise, or 2) Systemic hypotension due to pericardial fluid compromising cardiac function.

AV Fistula: A connection between the access artery and the accompanying vein that is demonstrated by arteriography or ultrasound and often characterized by a continuous bruit.

Infection Related to Device: Indicate if the patient experienced an infection related to the device.

MI: Indicate if the patient experienced an MI during the EP lab visit or after lab visit until discharge (or before any subsequent lab visits) as documented by:

NON ST ELEVATION MYOCARDIAL INFARCTION (NSTEMI)

AT LEAST ONE OF THE FOLLOWING BIOCHEMICAL INDICATORS for detecting myocardial necrosis must be present:

- 1) Troponin T or I: Maximal concentration of troponin T or I > the MI decision limit on at least one occasion during the first 24 hours after the index clinical event.
- 2) CK-MB: Maximal value of CK-MB > 2 x the upper limit of normal on one occasion during the first hours after the index clinical event. OR Maximal value of CK-MB, preferable CK-MB mass, > upper limit of normal on two successive samples.
- 3) Total CK: In the absence of availability of a troponin or CK-MB assay, total CK > 2 x the upper limit of normal, or the B fraction of CK may be employed, but these last two biomarkers are considerably less satisfactory than CK-MB.

AND ONE OF THE FOLLOWING:

- 1) Either ST segment depression or T wave abnormalities; or
- 2) Ischemic symptoms in the presence or absence of chest discomfort. Ischemic symptoms may include:
 - a) unexplained nausea and vomiting; or
 - b) persistent shortness of breath secondary to left ventricular failure; or
 - c) unexplained weakness, dizziness, lightheadedness, or syncope.

ST ELEVATION MYOCARDIAL INFARCTION (STEMI)

AT LEAST ONE OF THE FOLLOWING BIOCHEMICAL INDICATORS for detecting myocardial necrosis must be present (Reference Control Limits as above):

- 1) Troponin T or I
- 2) CK-MB
- 3) Total CK

AND ONE OF THE FOLLOWING ECG CHANGES:

- 1) ST-segment elevation: New or presumed new ST segment elevation at the J point in two or more contiguous leads with the cut-off points ≥ 0.2 mV in leads V1, V2, or V3, or ≥ 0.1 mV in other leads; OR
- 2) Development of any Q wave in leads V1 through V3, or the development of a Q-wave $>$ or $=$ to 30 ms (0.03s) in leads I, II, aVL, aVF, V4, V5, or V6. (Q wave changes must be present in any two contiguous leads, and be $>$ or $=$ to 1mm in depth.)

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