Important Differences in Mode of Death Between Men and Women With Heart Failure Who Would Qualify for a Primary Prevention Implantable Cardioverter-Defibrillator

Robert W. Rho, MD; Kristen K. Patton, MD; Jeanne E. Poole, MD; John G. Cleland, MD; Ramin Shadman, MD; Inder Anand, MD; Aldo Pietro Maggioni, MD; Peter E. Carson, MD; Karl Swedberg, MD; Wayne C. Levy, MD;

**Background**—Whether sex differences in implantable cardioverter-defibrillator (ICD) benefit exist remains unanswered. We evaluated sex differences in mode of death among a large cohort of ambulatory heart failure patients who meet criteria for a primary prevention ICD.

**Methods and Results**—Patients from 5 trials or registries were included if they met American College of Cardiology/American Heart Association/Heart Rhythm Society guideline criteria for implantation of a primary prevention ICD. We investigated the potential sex differences in total deaths and total deaths by mode of death. The relationship between the estimated total mortality and mode of death by percentage of total mortality was also analyzed by sex. The Seattle Heart Failure Model was used to estimate total mortality in this analysis. A total of 8337 patients (1685 [20%] women) met inclusion criteria. One-year mortality was 10.8±0.3%. In women, the age-adjusted all-cause mortality was 24% lower (hazard ratio [HR], 0.76; confidence interval [CI], 0.68–0.85; P<0.0001), the risk of sudden death was 32% lower (HR, 0.68; CI, 0.58–0.68; P<0.0001), but no significant difference in pump failure death was observed. Throughout a range of total mortality risk, women had a 20% lower all-cause mortality (HR, 0.80; CI, 0.71–0.89; P<0.0001) and 30% fewer deaths that were sudden (HR, 0.70; CI, 0.59–0.82; P<0.0001) compared with men.

**Conclusions**—Women with heart failure have a lower mortality than men, and fewer of those deaths are sudden throughout a spectrum of all-cause mortality risk. These data provide a plausible reason for and thus support the possibility that sex differences in ICD benefit may exist. (Circulation. 2012;126:2402-2407.)

**Key Words:** cardiac resynchronization therapy ■ death, sudden ■ defibrillators ■ heart failure ■ pump failure

Women are poorly represented in clinical trials from which current standards of care and treatment guidelines are derived. Men and women are known to differ in the pathophysiology, causes, clinical characteristics, and natural history of heart disease, but sex-specific treatment strategies are rarely used in cardiovascular medicine. Current practice guidelines for appropriate device therapies for heart failure patients are no exception.1 Recently, several meta-analyses suggested that women with heart failure might benefit less than men from implantable cardioverter-defibrillator (ICD) therapy for reduction in all-cause mortality.2-4 In contrast, a sex analysis of Multi-center Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy (MADIT-CRT) demonstrated that women with mild heart failure symptoms and a wide QRS benefit more from cardiac resynchronization therapy than similarly selected men.5-7 Accordingly, we investigated differences in modes of death among ambulatory men and women with heart failure who would be candidates for ICD therapy according to the American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) guidelines.1 Because the proportion of sudden, pump failure, and other deaths have been demonstrated to be influenced by the estimated total mortality risk, we evaluated mode of death across a spectrum of estimated total mortality risk. The Seattle Heart Failure Model (SHFM), a validated mortality risk model, was used to define total mortality risk.8,9

**Clinical Perspective on p 2407**

**Methods**

**Study Population**
We used a participant-level deidentified database of prospectively collected data from ambulatory heart failure patients with predominantly
Determination of the Seattle Heart Failure Model Score

The development of the SHFM score has been described previously. Briefly, the SHFM was derived from a cohort of 1038 heart failure patients from 5 studies, providing 23037 patient-years of observation, and included variables such as age, sex, systolic blood pressure, cause, NYHA class, left ventricular ejection fraction, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, β-adrenergic receptor blocker, carvedilol, digoxin, statin, furosemide daily dose, serum sodium, and creatinine. The SHFM has been validated in other heart failure populations, demonstrating its accuracy for predicting all-cause mortality and mode of death. The modified SHFM score, shown to predict ICD benefit in the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), was used in this analysis. We calculated SHFM score excluding patient sex (the variable of interest) in each patient and analyzed differences in mode of death by sex as a function of SHFM risk score. The SHFM score was rounded to the nearest integer from 0 to 2. A SHFM score of 0, 1, and 2 have low (≈10%–15%), intermediate (≈10%–15%), and high (≈25%) annual mortality rates, respectively.

Determination of Mortality and Mode of Death

Mortality and mode of death were adjudicated by independent central adjudication committees except for the UW cohort, which was adjudicated by one investigator (W.C.L.). Mode of death was classified as sudden death (unexpected death in a clinically stable patient within 1 hour of symptom onset, from a documented or presumed cardiac arrhythmia, and without a clear noncardiovascular cause), pump failure death (progressively reduced cardiac output and failure of organ perfusion), and other death (not adjudicated as either sudden or pump failure death).

Statistical Analysis

Baseline demographic and clinical variables were compared between men and women with the χ² test for categorical variables and t tests for continuous variables. Cause-specific mortality was evaluated with the Fine and Gray competing risk proportional hazards model (Stata 11.2). For categorical analyses, the SHFM score for each patient was rounded to the nearest integer between 0 and 2, representing low, intermediate, and high-risk subgroups. Kaplan–Meier methods were used to evaluate survival according to the SHFM score, with significance of differences evaluated with the log rank test. Cox proportional hazards analyses were used to estimate relative risk (hazard ratios [HRs]) according to the SHFM. For all tests, a probability value of <0.05 was considered significant. Relevant to the selection of device therapies aimed at sudden death (implantable cardioverter defibrillator or pump failure death (cardiac resynchronization therapy), we evaluated the proportion of total deaths for sudden, pump failure, and other deaths by sex and SHFM risk score in a logistic regression model that included only those who died. Statistical analysis were performed with SPSS 19.0 and Stata 1.2. A probability value of <0.05 was considered significant.

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Mean±SD</th>
<th>Total (n=10387)</th>
<th>Women (n=1697)</th>
<th>Men (n=8690)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62.6±11.1</td>
<td>64.0±11.7</td>
<td>62.3±11.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ischemic cause, %</td>
<td>56%</td>
<td>43%</td>
<td>59%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>25.1±6.5</td>
<td>24.9±6.5</td>
<td>25.2±6.5</td>
<td>0.07</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>123.7±18.9</td>
<td>125.7±19.6</td>
<td>123.3±18.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Furosemide, mg/kg/day</td>
<td>0.9±1.0</td>
<td>1.1±1.2</td>
<td>0.9±0.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NYHA Class II, %</td>
<td>51%</td>
<td>43%</td>
<td>53%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ACE I</td>
<td>93%</td>
<td>90%</td>
<td>94%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ARB</td>
<td>29%</td>
<td>29%</td>
<td>28%</td>
<td>0.60</td>
</tr>
<tr>
<td>β-blockers</td>
<td>50%</td>
<td>49%</td>
<td>52%</td>
<td>0.03</td>
</tr>
<tr>
<td>Potassium sparing diuretics</td>
<td>6.5%</td>
<td>7%</td>
<td>6%</td>
<td>0.19</td>
</tr>
<tr>
<td>Statins</td>
<td>26%</td>
<td>23%</td>
<td>26%</td>
<td>0.002</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.3±0.4</td>
<td>1.1±0.4</td>
<td>1.3±0.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Serum sodium, mg/dL</td>
<td>139.5±3.3</td>
<td>139.7±3.3</td>
<td>139.4±3.3</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; NYHA, New York Heart Association; ACE, angiotensin-converting enzyme; and ARB, angiotensin receptor blocker.

Results

Baseline Characteristics

Of 1038 patients evaluated for inclusion into the study, 55 patients (5.5%) with NYHA class I or IV heart failure symptoms, 1084 (10.8%) patients with left ventricular ejection fraction >35%, 130 (1.3%) patients who received a heart transplant, and 30 (0.3%) patients who had an ICD at baseline were excluded, leaving 8337 patients eligible for analysis, of which 1685 (20%) were women. Women were older and were less likely to have ischemic heart disease (Table 1). Baseline characteristics by trial are shown in Table 1 in the online-only Data Supplement.

Mortality

Total mortality for all patients over a median follow-up period of 2.4 years was 26.3%. Overall, 12.7% of patients died suddenly (48% of all deaths), 7.9% died of pump failure (30% of all deaths), and 5.7% of patients died in other ways (22% of all deaths); Table 2. Overall one-year mortality for all-cause mortality was 10.8%±0.3%, whereas 5.3±0.3% died suddenly, 3.1±0.2% died of pump failure and 2.8±0.2% had other causes of death.

Age adjusted all-cause mortality was 24% lower for women than for men (HR, 0.76; 95% confidence interval [CI] 0.68–0.85; P<0.0001). Age adjusted mortality from sudden death was 32% lower for women compared with men (HR, 0.68; CI, 0.58–0.80; P<0.0001), but mortality from pump failure was similar in men and women (HR, 0.95; CI, 0.78–1.14; P=0.56). Mortality from other causes was 22% lower in women (HR 0.78; CI, 0.61–0.98; P=0.037). The unadjusted, age-adjusted, age- and SHFM-adjusted, and the fully adjusted Fine and Gray proportional hazard ratio for female sex are shown in Table 3.

Analysis by Seattle Heart Failure Score

Analysis by SHFM score demonstrated that sex differences in mode of death remain across the spectrum of mortality risk.
using the estimated mortality as a continuous score. For any SHFM score, women had a 20% lower risk of all-cause mortality compared with men (HR, 0.80; 95% CI, 0.71–0.89; P < 0.001). The SHFM adjusted risk of sudden death in women was 30% lower compared with men (HR, 0.70; CI, 0.59–0.82; P < 0.0001), and the risk of other death was 21% lower in women (HR, 0.79; 95% CI, 0.62–1.00; P = 0.052) when compared with men. Similar results were observed in the fully adjusted model (Table 3).

Sex Differences in Mode of Death as a Proportion of Total Mortality

In men and in women, as the SHFM score increased (increasing risk of overall mortality), the proportion of sudden death decreased (odds ratio, 0.66; P < 0.0001) and the proportion of pump failure death increased (odds ratio, 1.97; P < 0.0001). The Kaplan–Meier observed annual mortality and the percentage of deaths attributed to sudden, pump failure, and other deaths for women versus men by SHFM scores is shown in Figures 1 to 3. For any SHFM score, the proportion of sudden death is 30% lower (P = 0.022) for women compared with men, and the proportion of pump failure death is 54% higher (P = 0.0004).

**Discussion**

In this large cohort of patients with heart failure who were potentially eligible for a primary prevention ICD, ≈5% of patients died suddenly each year. However, the annual rate was somewhat lower in women (3.9%) compared with men (5.7%). For all SHFM risk groups (low, intermediate, and high), women had a lower all-cause mortality compared with men. Although women have a better overall prognosis than men, the mortality rate for women remains high. The overall 1-year total mortality rate of 9.1% for women in this study is higher than for men, with 5.7%.

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**Table 2. Mortality by Mode of Death for the Total Population and by Gender**

<table>
<thead>
<tr>
<th>SHFM Score</th>
<th>Total Mortality</th>
<th>Sudden Death</th>
<th>Pump Failure Death</th>
<th>Other Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>2.39</td>
<td>26.3%</td>
<td>12.7%</td>
<td>7.9%</td>
</tr>
<tr>
<td>Men</td>
<td>2.37</td>
<td>27.2%</td>
<td>13.5%</td>
<td>7.8%</td>
</tr>
<tr>
<td>Women</td>
<td>2.46</td>
<td>22.6%</td>
<td>9.6%</td>
<td>8.1%</td>
</tr>
</tbody>
</table>

**Table 3. Fine and Gray proportional Hazards Ratio for Outcome Among Women**

<table>
<thead>
<tr>
<th>HR (95% CI)</th>
<th>P Value</th>
<th>All-Cause Mortality</th>
<th>Sudden Death</th>
<th>Pump Failure Death</th>
<th>Other Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>0.81</td>
<td>0.69</td>
<td>1.03</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>0.72–0.90</td>
<td>0.0001</td>
<td>(0.59–0.82)</td>
<td>(0.85–1.24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>0.76</td>
<td>0.68</td>
<td>0.95</td>
<td>0.78</td>
<td></td>
</tr>
<tr>
<td>0.68–0.85</td>
<td>0.0001</td>
<td>(0.58–0.80)</td>
<td>(0.78–1.14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 3</td>
<td>0.80</td>
<td>0.70</td>
<td>1.06</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>0.71–0.89</td>
<td>0.0002</td>
<td>(0.59–0.82)</td>
<td>(0.87–1.28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 4</td>
<td>0.79</td>
<td>0.68</td>
<td>1.01</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>0.71–0.89</td>
<td>&lt;0.0001</td>
<td>(0.57–0.81)</td>
<td>(0.583–1.23)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Model 1:** Unadjusted hazard ratio for women.

**Model 2:** Adjusted for age.

**Model 3:** Adjusted for age and SHFM (excluding patient sex as a variable).

**Model 4:** Adjusted for age, ischemic etiology, NYHA class, EF, SBP, ACEI/ARB, beta blocker, aldosterone blocker, statin, loop diuretic daily dose, serum sodium and creatinine.

HR indicates hazard ratio; CI, confidence interval.
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... angiotensin-converting enzyme blocker, reflecting enrollment in trials before the known benefit of β-blockers in heart failure.

Our findings provide important insight into recent data that raise the possibility that women may experience less appropriate shocks and derive less survival benefit from primary prevention ICDs compared with men. In a meta-analysis of 5 trials that randomized patients to an ICD versus optimal medical therapy, Santanelli et al demonstrated an ICD survival benefit in men (HR, 0.6; 95% CI, 0.57–0.80; \( P < 0.001 \)) but no benefit in women (HR, 0.84; 95% CI, 0.59–1.19; \( P = 0.33 \)). Significantly fewer appropriate ICD therapies were observed in women compared with men in this study (HR, 0.63; 95% CI, 0.49–0.82; \( P < 0.001 \), I2=0%).

Similar findings were reported in 2 other meta-analyses. Although the results of these studies require prospective validation, our analysis suggests that women are less likely to die suddenly and therefore have less opportunity to benefit from an ICD.

The differences in mode of death observed in this study may have been attributed, in part, to differences in the baseline characteristics observed in our study. Women are less likely to have ischemic cardiomyopathy as a cause of their left ventricular dysfunction. However, despite this consistent finding, sex-differences in arrhythmia susceptibility after an acute myocardial infarction have been demonstrated. In an analysis of pooled patient data from the placebo arms of 5 large myocardial infarction studies, Yap et al demonstrated that all-cause mortality was high and remained high for 2 years after an MI. In men, the incidence of sudden death exceeded other modes of death for 2 years after their index myocardial infarction. In contrast, for women, sudden death exceeded other modes of death for only 6 months after their index myocardial infarction.

An abundance of basic and clinical data have demonstrated sex-differences in arrhythmia susceptibility. Animal studies have demonstrated sex differences in potassium channel kinetics, calcium sensitivity and handling, autonomic modulation, and differences in Na–Ca exchanger that may lower susceptibility to triggered activity. In humans, studies evaluating out-of-hospital cardiac arrests demonstrate that women present more commonly with asystole and pulseless electric activity, whereas men are more likely to be found in ventricular tachycardia or ventricular fibrillation.

**Implications for Cardiac Resynchronization Therapy**

The results of our study also provide a plausible reason for the recent observation that women may derive more benefit from cardiac resynchronization therapy compared with men. A retrospective analysis of the MADIT-CRT demonstrated that women randomized to cardiac resynchronization therapy–ICD versus ICD had a 69% reduction in death or heart failure (HR, 0.31; \( P < 0.001 \)) compared with a 28% reduction in men (HR, 0.72; \( P < 0.001 \)). The RAFT-CRT trial reported similar findings, with a 45% reduction in death or heart failure in women versus a 20% reduction in men. Although our study demonstrated no difference in age-adjusted pump...
failure death between men and women, because total mortality was lower in women, the proportion of deaths attributable to pump failure was 54% higher in women compared with men. Given this finding, women would experience proportionately more benefit from cardiac resynchronization therapy, a therapy that has been proven to significantly decrease mortality from pump failure deaths.32

Mode of Death and Seattle Heart Failure Model Estimated Total Mortality Risk
An important finding in this study is that throughout a spectrum of SHFM-estimated total mortality risk, as risk increases the proportion of sudden death decreases and the proportion of pump failure death increases for both men and women. However, for any SHFM total mortality risk score, the proportion of sudden death is 30% lower for women compared with men, and the proportion of pump failure death is 54% higher. This study supports the need for prospective randomized studies aimed at refining selection criteria for women who may benefit from an ICD and from cardiac resynchronization therapy.

Limitations
Some limitations to this study do exist. It is a given that assignment of mode of death is difficult. In addition, it is well understood that not all sudden deaths are attributable to ventricular arrhythmias. Our database was derived from prospectively collected patient level data from 5 randomized trials or heart failure registries. Mode of death in each of the published clinical trials was adjudicated by an independent central committee using a modified Hinkle-Thaler classification and are reported in each of the clinical trials. In one of the registries (University of Washington cohort) mode of death was assigned by a single investigator (W.C.L.) using similar Hinkle-Thaler methodology. Mode of death classification is often difficult and is a limitation of all published studies evaluating mode of death in various populations. Another potential limitation is that our patient data are obtained from studies with differences in inclusion criteria, inclusion of randomized study patients selected to evaluate specific treatments, and inclusion of registry data. However, these factors were addressed in our analysis by merging the data at the patient level and subsequently selecting patients by ICD eligibility criteria (NYHA class II and III and ejection fraction ≤35%). This methodology allowed for use of and adjustment for differences in patient demographic data, medication use, and outcomes data available from each study. The percentage of women in our study population is similar to the percentage of women represented in randomized ICD studies (MADIT II (19%)20 and SCD-HeFT (30%)32 and the Ontario ICD registry (21%)).31

Conclusions
In this large cohort of heart failure patients who potentially fulfilled current eligibility criteria for implantation of an ICD for primary prevention of sudden death, significant differences in mode of death are observed between sexes, with a lower proportional risk for sudden death and higher proportional risk for pump failure death in women compared with men. These sex differences in modes of death exist throughout a spectrum of SHFM-estimated total mortality risk and may help explain possible differences between men and women in the benefits of ICD and cardiac resynchronization therapy. Our findings support the need for focused research on optimal risk stratification and treatment of patients with heart failure who take into account the patient’s sex.

Disclosures
Dr Rho has received speaking honoraria and is a consultant for St. Jude Medical. Dr Poole received speaking honoraria from Medtronic, Boston Scientific, Biotronik, and St. Jude Medical. Dr Levy has received research grant support from the National Institutes of Health, Epocrates, HeartWare, Thoratec, and General Electric.

References


**CLINICAL PERSPECTIVE**

Multiple randomized clinical trials have demonstrated that ambulatory heart failure with moderate heart failure symptoms and an ejection fraction of <35% derive a survival benefit from an implanted cardiac defibrillator for primary prevention of sudden death. The implantable cardioverter-defibrillator (ICD) can be life-saving to patients at risk for sudden death attributable to ventricular arrhythmias. Recently published meta-analysis have raised the possibility that women may not benefit as much from ICDs and have less appropriate ICD shocks compared with men with heart failure. The possibility that women may not derive as much benefit from an ICD is plausible, as it is well understood that men and women differ significantly in the epidemiology, pathophysiology, and natural history of heart failure. Further, randomized studies evaluating the role of the ICD for primary prevention of sudden death are not unlike most studies in heart failure in that there is a significant underrepresentation of women in these studies. Relevant to this question, we evaluated the sex differences in mode of death in 8337 ambulatory heart failure patients, including 1685 (20%) women, who would qualify for a primary prevention ICD. Although age-adjusted total mortality was 24% lower in women compared with men, the annual mortality for women in this study was significant (9.1%). When compared with men, women were 31% less likely to die of sudden death. These findings provide a plausible reason for potential differences in ICD benefit between men and women and lend further support for the need for randomized studies aimed at defining the role of the ICD in the primary prevention of sudden death in women.
Important Differences in Mode of Death Between Men and Women With Heart Failure
Who Would Qualify for a Primary Prevention Implantable Cardioverter-Defibrillator
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Anand, Aldo Pietro Maggioni, Peter E. Carson, Karl Swedberg and Wayne C. Levy

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An erratum has been published regarding this article. Please see the attached page for:
/content/127/14/e541.full.pdf

Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2012/10/15/CIRCULATIONAHA.111.069245.DC1

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In the article by Rho et al, “Important Differences in Mode of Death Between Men and Women With Heart Failure Who Would Qualify for a Primary Prevention Implantable Cardioverter-Defibrillator,” which was published in the November 13, 2012 issue of the journal (*Circulation*, 2012;126:2402-2407), an error occurred. The sudden death variable used by the authors in one of the 5 trials used in the manuscript was not “sudden death”, but was rather “sudden death without worsening heart failure death.” This error led to a lower overall sudden death rate as well as a higher other death rate (defined as not sudden or pump failure death) than would have been found had the relevant variable from one trial not been miscoded.

Despite this error, with its correction, there are no meaningful differences in either the lower proportion of sudden death in women vs. men (32% new vs. 31% original) or in the conclusions of the manuscript.

The major finding that has changed is that the proportion of sudden death overall has increased overall (48.4% current vs. 39.9% original), and in both women and men (Table 2 and Figure 2). Also, the hazard ratios in the Fine and Gray model are changed minimally (Table 3). Finally, Figure 3 has a lower proportion of other deaths; though this was not the focus of the manuscript.

The authors have supplied the corrected values for Table 2 & 3 and Figure 1 (sudden death). Also, though the findings in Figure 3 were not a focus of the manuscript, they have also supplied a corrected Figure 3 (other death).

Percentages, hazard ratios, and confidence intervals have been updated throughout the abstract, results, and discussion.

The corrections have been made in the current online version of the manuscript. The authors regret the errors.

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### Table Supplement 1

**Baseline Characteristics By Trial**

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<thead>
<tr>
<th></th>
<th>PRAISE1 (n=921)</th>
<th>University of Washington (n=72)</th>
<th>Val-HeFT (n=4276)</th>
<th>Italian Heart Failure Registry (n=459)</th>
<th>COMET (n=2609)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>64.6±11.3</td>
<td>51.0±10.8</td>
<td>62.7±11.1</td>
<td>63.6±11.4</td>
<td>62.0±11.1</td>
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<tr>
<td><strong>Female (%)</strong></td>
<td>22%</td>
<td>20%</td>
<td>20%</td>
<td>19%</td>
<td>23%</td>
</tr>
<tr>
<td><strong>Ischemic etiology (%)</strong></td>
<td>63%</td>
<td>26%</td>
<td>56%</td>
<td>51%</td>
<td>53%</td>
</tr>
<tr>
<td><strong>Ejection Fraction</strong></td>
<td>21.0±5.7</td>
<td>24.3±6.9</td>
<td>25.4±6.3</td>
<td>27.7±5.5</td>
<td>25.7±6.5</td>
</tr>
<tr>
<td><strong>SBP (mm Hg)</strong></td>
<td>118.0±17.3</td>
<td>104.8±15.5</td>
<td>123.6±18.4</td>
<td>125.9±20.8</td>
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<tr>
<td><strong>Furosemide (mg/kg/day)</strong></td>
<td>1.4±1.3</td>
<td>1.8±2.0</td>
<td>0.8±1.1</td>
<td>0.9±1.1</td>
<td>1.0±0.4</td>
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<tr>
<td><strong>NYHA Class II (%)</strong></td>
<td>0%</td>
<td>43%</td>
<td>62%</td>
<td>60%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>ACE I (%)</strong></td>
<td>100%</td>
<td>76%</td>
<td>93%</td>
<td>89%</td>
<td>91%</td>
</tr>
<tr>
<td><strong>ARB (%)</strong></td>
<td>0%</td>
<td>29%</td>
<td>51%</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td><strong>Beta Blockers (%)</strong></td>
<td>0%</td>
<td>82%</td>
<td>34%</td>
<td>34%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Potassium sparing diuretics (%)</strong></td>
<td>3%</td>
<td>28%</td>
<td>5%</td>
<td>0%</td>
<td>11%</td>
</tr>
<tr>
<td><strong>Statins (%)</strong></td>
<td>8%</td>
<td>32%</td>
<td>32%</td>
<td>15%</td>
<td>22%</td>
</tr>
<tr>
<td><strong>Creatinine (mg/dL)</strong></td>
<td>1.4±0.5</td>
<td>1.2±0.4</td>
<td>1.3±0.3</td>
<td>1.3±0.6</td>
<td>1.2±0.4</td>
</tr>
<tr>
<td><strong>Serum sodium (mg/dL)</strong></td>
<td>139.2±3.8</td>
<td>136.8±3.3</td>
<td>139.4±3.0</td>
<td>140.2±3.7</td>
<td>139.7±3.3</td>
</tr>
<tr>
<td><strong>Time of observation (years)</strong></td>
<td>2.76±0.71</td>
<td>3.23±1.13</td>
<td>1.88±0.66</td>
<td>0.92±0.21</td>
<td>5.96±1.57</td>
</tr>
</tbody>
</table>