

Age- and Gender-Related Differences in Quality of Care and Outcomes of Patients Hospitalized With Heart Failure (from OPTIMIZE-HF)

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Previous studies have suggested that female and elderly patients with heart failure (HF) are less likely to receive guideline-recommended therapies, but these studies have involved select patient populations. We evaluated the differences in medical care and patient outcomes by age and gender among a broad cohort of hospitalized patients with HF. The Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF) is a registry and performance-improvement program involving 48,612 patients with HF from 259 hospitals. The data were analyzed by gender, age <75 years, and age ≥75 years. Appropriate angiotensin-converting enzyme inhibitor/angiotensin receptor blocker and β-blocker use were similar between women and men (p = 0.244 and p = 0.237, respectively). However, compared with men, fewer women received hospital discharge instructions (p <0.001) and the length of stay was longer (p <0.001). Risk-adjusted in-hospital and postdischarge mortality were similar. All guideline-recommended cardiac medications were prescribed less frequently at discharge to eligible patients ≥75 than to those <75 years (all p <0.001). Older age was independently associated with in-hospital and postdischarge mortality risk increases (76% and 62%, respectively; p <0.001 for both). In conclusion, among the OPTIMIZE-HF hospitals, female patients with HF generally received similar medical care and had similar risks of adverse clinical outcomes compared with male patients. Older patients with HF were less likely to receive guideline-recommended therapies and remained at greater risk of adverse outcomes. © 2009 Elsevier Inc. All rights reserved. (Am J Cardiol 2009;104:107–115)

Heart failure (HF) is a growing healthcare problem in the United States, currently afflicting >5 million patients, with another 550,000 new cases diagnosed annually.¹ The prevalence of HF in the population and the treatment these patients receive are influenced by both age and gender.² Previous studies have shown that women treated for HF are significantly less likely than men to be prescribed angiotensin-converting enzyme (ACE) inhibitors, and when ACE inhibitors are prescribed for women, they tend to be pre-

scribed at suboptimal doses.^{3,4} Age-related disparities also occur in HF, because elderly patients with HF have been shown to be undertreated with ACE inhibitors and β blockers, with doses frequently less than recommendations based on evidence from clinical trials.^{5,6} The clinical outcomes among female and elderly patients with HF have failed to improve at the same rate as those seen in male and younger patients with HF.^{7,8} It is unclear whether the reported age and gender differences for improvements in clinical outcomes reflect a dissimilarity in pathophysiology, a divergent

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response to treatment, or disparities in care. An evaluation of age- and gender-related patterns of HF care and outcomes is important, given the efforts underway to address disparities in healthcare.

Methods

The Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF) is a large registry and performance-improvement initiative for patients hospitalized with HF. The details of the OPTIMIZE-HF design have been previously described.⁹ From March 2003 to December 2004, eligible adult patients hospitalized with HF at 259 participating hospital centers in the United States were enrolled in the OPTIMIZE-HF prospective registry. The HF patient registry was used to capture detailed data on various patient characteristics, including demographics, medical history, signs and symptoms, medications, contraindications or intolerance to medications, laboratory values, diagnostic testing results, procedures, discharge status, and adherence to performance indicators, using a Web-based information system. Participating hospitals had the ability to view the national aggregate hospital data, as well as daily patient and performance data benchmarked with similar hospitals. All regions of the United States were represented, and all types of institutions, from community hospitals to large, tertiary medical centers were included. A list of participating hospitals has been previously published.¹⁰ The sites had the option of participating in the follow-up data collection, and the protocol was approved by each participating center's institutional review board or through the use of a central institutional review board. A total of 91 hospitals provided 60- to 90-day follow-up data, and this cohort was demographically similar to the patients in the overall registry.^{10,11} The patients who participated in the follow-up data collection provided written informed consent before enrollment. Automated electronic data checks were used to prevent out-of-range entry or duplicate patients. A database audit was performed, using predetermined criteria, of a random sample of 5% of the first 10,000 patients verified against source documents showing >99% concordance on 53% of the fields (118 of 223) and 95% concordance on 91% of the fields (205 of 223). Fields with <95% concordance were not used in the present analysis.^{10,11}

The OPTIMIZE-HF Process-of-Care Improvement Program provided participating hospitals with materials for improving treatment and discharge plans for optimal patient management and included evidence-based best practice algorithms (detailed algorithms on the indications, contraindications, dosing, and monitoring steps for each evidence-based HF therapy), along with comprehensive patient education materials and resources.⁹ These tools were based on published HF guidelines from the American College of Cardiology, the American Heart Association, and the Heart Failure Society of America (available from: <http://www.optimize-hf.org>).¹²⁻¹⁴ Registry participation did not require any alteration of treatment or hospital care, and entry of data into the registry was not contingent on the use of any particular therapeutic agent or treatment.

The hospital teams used HF case-ascertainment methods similar to those of the Joint Commission on Accreditation of Healthcare Organizations.¹⁵ The participants were screened for inclusion before hospital discharge or identified from administrative databases subsequent to discharge. Patients qualified for enrollment if they were hospitalized for episodes of new or worsening HF as the primary cause of admission or if significant HF symptoms developed during hospitalization for another primary diagnosis, with HF being the primary discharge diagnosis.⁹ Consecutive patients were enrolled irrespective of their ventricular function, including left ventricular systolic dysfunction, documented by a left ventricular ejection fraction <40% or qualitative moderate to severe dysfunction; HF symptoms in the setting of preserved left ventricular systolic function (diastolic dysfunction HF); or HF without left ventricular function measurement.¹²⁻¹⁴

The specific quality metrics examined in the present analysis included the use of evidence-based HF medicines (i.e., ACE inhibitor and/or angiotensin receptor blockers [ARBs] for left ventricular systolic dysfunction, aldosterone antagonists for left ventricular systolic dysfunction, β blockers for left ventricular systolic dysfunction, anticoagulation with warfarin for atrial fibrillation); Joint Commission on Accreditation of Healthcare Organizations core HF measures (i.e., complete discharge instructions, left ventricular ejection fraction assessment, discharge ACE inhibitor use in left ventricular systolic dysfunction, smoking-cessation counseling for patients who were current or recent smokers), and outcomes in-hospital (i.e., length of stay, in-hospital mortality) and at 60- to 90 days of follow-up (i.e., rehospitalization, mortality). Quality metrics included only patients eligible without documented contraindications or intolerance. Aldosterone antagonist use was reported only in men with creatinine of ≤ 2.5 mg/dl, women with creatinine of ≤ 2.0 mg/dl, and patients with potassium < 5.0 mEq/L.

All statistical analyses were conducted independently by the Duke Clinical Research Institute (Durham, North Carolina). The data are reported as the number and frequency of eligible patients treated at hospital discharge, excluding patients with documented intolerance or contraindications to specific therapies. HF medication use and contraindications or intolerance were assessed at discharge from the index hospitalization. Age and gender were analyzed according to age <75 or ≥ 75 years and male or female, respectively. Patients <18 or >105 years were excluded. The patient characteristics and evidence-based treatments at hospital discharge were compared using the Pearson chi-square test for categorical variables and the Wilcoxon rank sum test for continuous variables. Models of in-hospital mortality, mortality from hospital discharge to 90 days, and the combination of postdischarge mortality or rehospitalization were developed to determine significant factors to use when applying adjusted models.^{10,11} Baseline clinical and treatment factors were applied to the model selections. To model in-hospital mortality, 45 potential predictor variables were used in a logistic model. To model postdischarge mortality in the follow-up period, 19 potential predictor variables were used in a Cox proportional hazards model. To model rehospitalization and the combination of postdis-

Table 1
Patient characteristics at admission stratified by sex

| Characteristic | Total Population (n = 48,612) | Males (n = 23,537; 48.4%) | Women (n = 25,075; 51.6%) | p Value |
|--|----------------------------------|------------------------------|------------------------------|---------|
| Age (yrs) | | | | |
| Mean (SD) | 73.2 (14.0) | 70.8 (13.9) | 75.4 (13.6) | |
| Median (IQR) | 75.9 (64.6, 83.4) | 73.3 (62.0, 81.3) | 78.2 (67.8, 85.1) | <0.001 |
| Race | | | | |
| White | 74.1% | 74.2% | 74.1% | |
| Black | 17.7% | 17.3% | 18.1% | 0.004 |
| Ischemic etiology of HF | 45.7% | 53.3% | 38.6% | <0.001 |
| LVEF, mean (SD) (n = 36,115) | 39.0% (17.6) | 34.2% (16.2) | 43.7% (17.8) | <0.001 |
| Ejection fraction <40% | 51.8% | 63.0% | 40.4% | <0.001 |
| Medical history | | | | |
| Insulin-treated diabetes | 16.6% | 16.0% | 17.2% | <0.001 |
| Noninsulin-treated diabetes | 24.9% | 25.5% | 24.3% | 0.002 |
| Hypertension | 70.9% | 67.5% | 74.2% | <0.001 |
| Coronary artery disease | 49.5% | 55.0% | 44.4% | <0.001 |
| Hyperlipidemia | 32.1% | 34.3% | 30.1% | <0.001 |
| Atrial arrhythmia | 30.8% | 31.3% | 30.3% | 0.023 |
| Chronic obstructive pulmonary disease | 27.6% | 28.8% | 26.4% | <0.001 |
| Chronic renal failure | 19.6% | 22.5% | 16.8% | <0.001 |
| Anemia | 17.6% | 15.2% | 19.8% | <0.001 |
| Peripheral vascular disease | 13.7% | 15.1% | 12.3% | <0.001 |
| Previous cerebral vascular accident or transient ischemic attack | 15.5% | 14.7% | 16.4% | <0.001 |
| Thyroid abnormality | 15.0% | 9.2% | 20.5% | <0.001 |
| Pulmonary reactive airway disease | 5.6% | 4.4% | 6.8% | <0.001 |
| Liver disease | 1.6% | 2.1% | 1.2% | <0.001 |
| Depression | 10.6% | 8.8% | 12.3% | <0.001 |
| Cigarette smoker in past year | 16.5% | 20.8% | 12.4% | <0.001 |
| Admission physical findings | | | | |
| Weight, mean (SD), (kg) | 82.5 (26.2) | 89.5 (25.4) | 75.9 (25.2) | <0.001 |
| Rales | 64.0% | 62.7% | 65.3% | <0.001 |
| Jugular venous pressure elevation | 32.7% | 34.7% | 30.8% | <0.001 |
| Lower extremity edema | 64.6% | 65.8% | 63.5% | <0.001 |
| SBP, mean (SD), (mm Hg) | 142.7 (32.9) | 138.8 (32.2) | 146.3 (33.2) | <0.001 |
| DBP, mean (SD), (mm Hg) | 76.4 (19.1) | 77.1 (19.0) | 75.8 (19.2) | <0.001 |
| Heart rate, mean (SD), (beat/min) | 86.6 (21.4) | 86.1 (21.3) | 87.0 (21.6) | <0.001 |
| Admission laboratory values | | | | |
| Hemoglobin, mean (SD), (g/dl) | 12.1 (2.0) | 12.5 (2.1) | 11.8 (1.9) | <0.001 |
| Serum creatinine, mean (SD), (mg/dl) | 1.8 (1.6) | 1.9 (1.7) | 1.6 (1.4) | <0.001 |
| B-type natriuretic peptide, median (IQR), (pg/ml) | 804.0 (407–1670) | 855.0 (436–1780) | 762 (384–1580) | <0.001 |
| Troponin type I, median (IQR), (ng/ml) | 0.1 (0.1–0.3) | 0.1 (0.1–0.3) | 0.1 (0.0–0.3) | <0.001 |
| Sodium, mean (SD), (mEq/L) | 137.8 (4.8) | 137.9 (4.6) | 137.7 (4.9) | 0.008 |
| Admission medications | | | | |
| β -blocker | 53.1% | 54.7% | 51.6% | <0.001 |
| ACE inhibitor | 39.6% | 41.9% | 37.6% | <0.001 |
| Aldosterone antagonist | 7.1% | 8.0% | 6.3% | <0.001 |
| ARB | 11.7% | 10.5% | 12.9% | <0.001 |
| Digoxin | 23.4% | 25.8% | 21.2% | <0.001 |
| Diuretic | 65.7% | 65.1% | 66.2% | 0.016 |
| Lipid-lowering agent | 33.9% | 37.0% | 31.0% | <0.001 |
| Discharge physical findings | | | | |
| Rales | 15.4% | 15.0% | 15.9% | 0.009 |
| Jugular venous pressure elevation | 2.6% | 3.1% | 2.1% | <0.001 |
| Lower extremity edema | 26.9% | 28.5% | 25.4% | <0.001 |
| Discharge weight, mean (SD), (kg) | 80.2 (25.2) | 86.7 (24.4) | 73.9 (24.4) | <0.001 |
| Weight change, median (IQR), (kg) | −2.0 (−4.5–0) | −2.3 (−5.0–0) | −1.4 (0.4–0) | <0.001 |
| SBP, mean (SD), (mm Hg) | 124.8 (22.4) | 122.5 (21.9) | 126.9 (22.7) | <0.001 |
| DBP, mean (SD), (mm Hg) | 66.8 (12.8) | 67.9 (12.9) | 65.7 (12.6) | <0.001 |
| Heart rate, mean (SD), (beats/min) | 76.4 (14.1) | 76.1 (14.2) | 75.9 (14.0) | 0.054 |
| Discharge laboratory values | | | | |
| Creatinine, mean (SD), (mg/dl) (n = 41,228) | 1.8 (1.4) | 1.9 (1.5) | 1.6 (1.3) | <0.001 |
| B-type natriuretic peptide, median (IQR), (pg/ml) (n = 13,303) | 559.0 (280–1180) | 612.0 (308–1300) | 516.0 (260–1080) | <0.001 |

SI conversion factor: to convert creatinine to micromoles per liter, multiply by 88.4.

DBP = diastolic blood pressure; IQR = interquartile range; SBP = systolic blood pressure; SI = International System of Units.

Table 2
Patient characteristics at admission stratified by age

| Characteristic | Total Population (n = 48,525) | Age <75 Yrs (n = 22,913; 47.2%) | Age ≥75 Yrs (n = 25,612; 52.8%) | p Value |
|--|----------------------------------|------------------------------------|------------------------------------|---------|
| Women | 25,029 (51.6%) | 10,031 (43.8%) | 14,998 (58.6%) | <0.001 |
| Race | | | | <0.001 |
| White | 74.2% | 63.3% | 83.9% | |
| Black | 17.7% | 27.6% | 8.8% | |
| Ischemic etiology of HF | 45.7% | 43.7% | 47.5% | <0.001 |
| LVEF, mean (SD) (n = 36,060) | 39.0% (17.6) | 35.9% (17.2) | 42.0% (17.5) | <0.001 |
| Ejection fraction <40% | 51.8% | 59.2% | 44.7% | <0.001 |
| Medical history | | | | |
| Insulin-treated diabetes | 16.6% | 22.1 | 11.7 | <0.001 |
| Noninsulin-treated diabetes | 24.9% | 27.3 | 22.8 | <0.001 |
| Hypertension | 70.9% | 71.9 | 70.1 | <0.001 |
| Coronary artery disease | 49.6% | 46.9 | 52.0 | <0.001 |
| Hyperlipidemia | 32.1% | 34.6 | 30.0 | <0.001 |
| Atrial arrhythmia | 30.8% | 21.7 | 39.0 | <0.001 |
| Chronic obstructive pulmonary disease | 27.6% | 27.8 | 27.4 | 0.258 |
| Chronic renal failure | 19.6% | 19.6% | 19.5% | <0.001 |
| Anemia | 17.6% | 15.2% | 19.8% | <0.001 |
| Peripheral vascular disease | 13.7% | 13.0% | 14.3% | <0.001 |
| Previous cerebral vascular accident or transient ischemic attack | 15.6% | 12.9% | 17.9% | <0.001 |
| Thyroid abnormality | 15.0% | 11.3% | 18.4% | <0.001 |
| Pulmonary reactive airway disease | 5.6% | 7.1% | 4.3% | <0.001 |
| Liver disease | 1.6% | 2.6% | 0.7% | <0.001 |
| Depression | 10.6% | 11.3% | 10.1% | |
| Cigarette smoker in past year | 16.5% | 27.8% | 6.5% | |
| Admission physical findings | | | | |
| Weight, mean (SD), (kg) | 82.5 (26.2) | 93.0 (29.1) | 73.1 (19.0) | <0.001 |
| Rales | 64.1% | 60.6% | 67.1% | <0.001 |
| Jugular venous pressure elevation | 32.7% | 32.1% | 33.3% | <0.001 |
| Lower extremity edema | 64.7% | 65.9% | 63.6% | <0.001 |
| Systolic blood pressure, mean (SD), (mm Hg) | 142.7 (32.9) | 143.7 (34.4) | 141.8 (31.5) | <0.001 |
| Diastolic blood pressure, mean (SD), (mm Hg) | 76.4 (19.1) | 79.7 (20.2) | 73.5 (17.6) | <0.001 |
| Heart rate, mean (SD), (beats/min) | 86.5 (21.4) | 88.9 (21.7) | 84.4 (21.0) | <0.001 |
| Admission laboratory values | | | | |
| Hemoglobin, mean (SD), (g/dl) | 12.1 (2.0) | 12.3 (2.2) | 12.0 (1.9) | <0.001 |
| Serum creatinine, mean (SD), | 1.8 (1.6) | 1.9 (1.9) | 1.6 (1.1) | <0.001 |
| B-type natriuretic peptide, median | 804.0 (407–1670) | 756.0 (367–1615) | 836.4 (440–1720) | <0.001 |
| Troponin type I, median (IQR), (ng/ml) | 0.1 (0.1–0.3) | 0.1 (0.1–0.3) | 0.1 (0.1–0.3) | 0.055 |
| Sodium, mean (SD), mEq/L | 137.8 (4.7) | 137.8 (4.6) | 137.7 (4.9) | 0.519 |
| Admission medications | | | | |
| β blocker | 53.1% | 54.2% | 52.2% | <0.001 |
| ACE inhibitor | 39.6% | 42.1% | 37.4% | <0.001 |
| Aldosterone antagonist | 7.1% | 8.6% | 5.8% | <0.001 |
| ARB | 11.7% | 11.4% | 12.0% | 0.024 |
| Digoxin | 23.4% | 22.1% | 24.5% | <0.001 |
| Diuretic | 65.7% | 62.9% | 68.1% | <0.001 |
| Lipid-lowering agent | 33.9% | 36.8% | 31.4% | <0.001 |
| Discharge physical findings | | | | |
| Rales | 15.4% | 12.5% | 18.1% | <0.001 |
| Jugular venous pressure elevation | 2.6% | 2.9% | 2.3% | <0.001 |
| Lower extremity edema | 27.0% | 28.9% | 25.2% | <0.001 |
| Weight, mean (SD), (kg) | 80.2 (25.2) | 90.2 (27.9) | 71.2 (18.3) | <0.001 |
| Weight change, median (IQR), (kg) | −2.0 (−4.5,0) | −2.0 (−5.0,0) | −1.8 (−4.0,0) | <0.001 |
| SBP, mean (SD), (mm Hg) | 124.8 (22.4) | 124.8 (22.8) | 124.8 (22.1) | 0.288 |
| DBP, mean (SD), (mm Hg) | 66.8 (12.8) | 69.1 (13.2) | 64.6 (12.0) | <0.001 |
| Heart rate, mean (SD), (beats/min) | 76.0 (14.1) | 77.2 (14.3) | 74.9 (13.8) | <0.001 |
| Discharge laboratory values | | | | |
| Creatinine, mean (SD), (mg/dl) (n = 41,156) | 1.8 (1.4) | 1.9 (1.7) | 1.6 (1.0) | <0.001 |
| B-type natriuretic peptide, median (IQR), (pg/ml) (n = 13,295) | 559.0 (280–1180) | 534.0 (250–1150) | 577.0 (301–1200) | <0.001 |

SI conversion factor: to convert creatinine to micromoles per liter, multiply by 88.4.

Abbreviations as in Table 1.

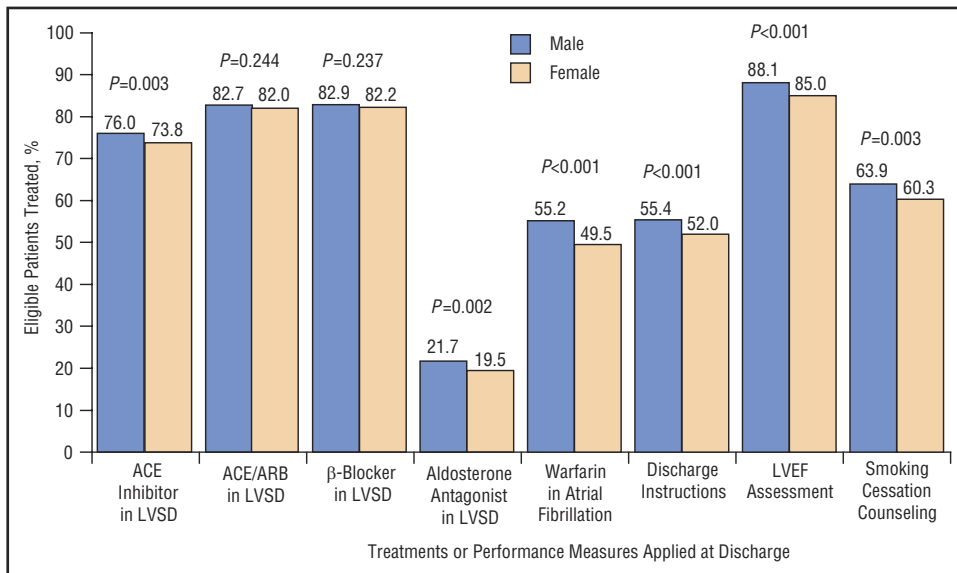


Figure 1. Quality of care for male and female patients in OPTIMIZE-HF. Implementation of evidence-based guideline recommendations at hospital discharge in patients, by gender. Treatment rates only for eligible patients without contraindications or intolerance. ACE inhibitor, ARB, β -blocker, and aldosterone antagonist use included only patients with left ventricular systolic dysfunction. Anticoagulation with warfarin use only for patients with atrial fibrillation. LVEF = left ventricular ejection fraction; LVSD = left ventricular systolic dysfunction.

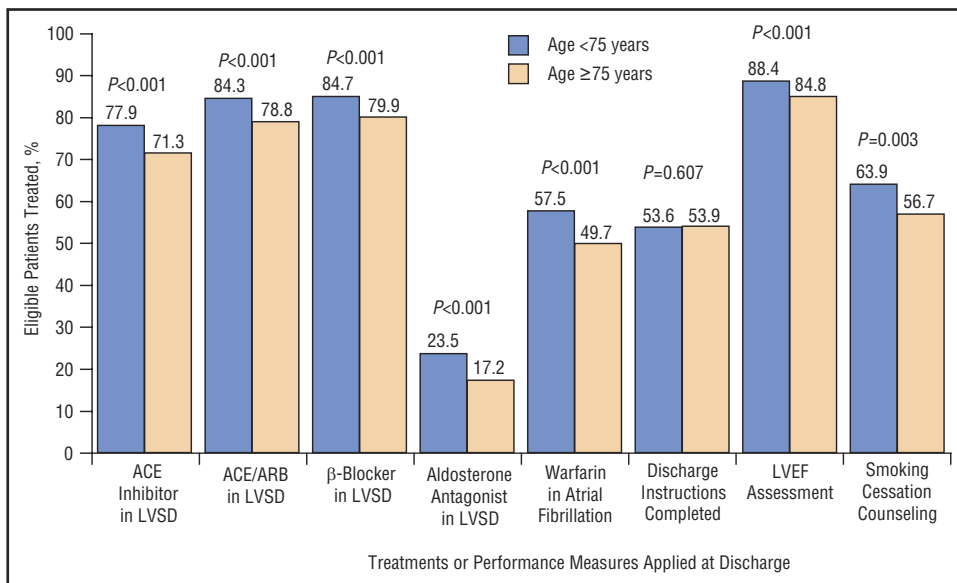


Figure 2. Quality of care for younger and older patients in OPTIMIZE-HF. Implementation of evidence-based guideline recommendations at hospital discharge in eligible patients, by patient age. Treatment rates only for eligible patients without contraindications or intolerance. ACE inhibitor, ARB, β -blocker, and aldosterone antagonists use included only patients with left ventricular systolic dysfunction (LVSD). Anticoagulation with warfarin use only for patients with atrial fibrillation. LVEF = left ventricular ejection fraction.

charge mortality or rehospitalization, 69 variables were used in a logistic model. To model conformity with quality-of-care measures, 71 to 93 variables were considered for each model. The assumption of linearity was checked in each model for the continuous variables using restricted cubic splines. When the relationship was nonlinear, appropriate transformations were applied. The assumption of proportionality was tested in the Cox models. Generalized estimating equations were used to account for the correlation of data within the same hospital in the adjusted models.

For all statistical analyses, Statistical Analysis Systems, version 8.2 (SAS Institute, Cary, North Carolina), was used.

Results

A total of 48,612 patients enrolled from 259 United States hospitals from March 1, 2003 to December 31, 2004, of whom 25,075 (51.6%) were women and 23,537 (48.4%) were men. The median age was 75.9 years; 47.2% were <75 years and 52.8% were \geq 75 years old. The baseline

Table 3
Association of sex and age and quality of care

| Quality Measures and Other Care Metrics | Women | | | | Age \geq 75 Yrs | | | |
|---|------------------|---------|------------------|---------|-------------------|---------|------------------|---------|
| | Unadjusted | | Adjusted | | Unadjusted | | Adjusted | |
| | OR (95% CI) | p Value | OR (95% CI) | p Value | OR (95% CI) | p Value | OR (95% CI) | p Value |
| HF-1: delivery of HF discharge instructions | 0.87 (0.84–0.91) | <0.001 | 0.96 (0.93–0.99) | 0.022 | 1.03 (0.98–1.08) | 0.196 | 1.01 (0.97–1.05) | 0.709 |
| HF-2: left ventricular function assessment | 0.80 (0.76–0.85) | <0.001 | 0.86 (0.81–0.92) | <0.001 | 0.75 (0.71–0.80) | <0.001 | 0.77 (0.71–0.83) | <0.001 |
| HF-3: ACE inhibitor at discharge for LVSD | 0.93 (0.86–1.00) | 0.054 | 0.95 (0.85–1.05) | 0.325 | 0.71 (0.66–0.76) | <0.001 | 0.89 (0.80–0.98) | 0.022 |
| HF-4: smoking cessation counseling | 0.88 (0.79–0.97) | 0.010 | 0.90 (0.80–1.00) | 0.054 | 0.75 (0.66–0.85) | <0.001 | 0.75 (0.66–0.85) | <0.001 |
| ACE inhibitor or ARB at discharge for LVSD | 0.98 (0.90–1.07) | 0.655 | 0.94 (0.84–1.05) | 0.266 | 0.73 (0.67–0.80) | <0.001 | 0.92 (0.82–1.04) | 0.192 |
| β -blocker at discharge for LVSD | 0.99 (0.91–1.08) | 0.790 | 0.98 (0.87–1.11) | 0.789 | 0.73 (0.67–0.79) | <0.001 | 0.80 (0.72–0.89) | <0.001 |
| Aldosterone antagonist at discharge for LVSD | 0.92 (0.84–1.00) | 0.054 | 0.89 (0.81–0.99) | 0.031 | 0.69 (0.63–0.75) | <0.001 | 0.83 (0.75–0.92) | <0.001 |
| Warfarin at discharge for atrial fibrillation | 0.84 (0.78–0.90) | <0.001 | 0.84 (0.78–0.92) | <0.001 | 0.76 (0.70–0.82) | <0.001 | 0.75 (0.68–0.83) | <0.001 |

CI = confidence interval; HF = heart failure; LVSD = left ventricular systolic dysfunction; OR = odds ratio.

Table 4
Clinical outcomes of hospital and follow-up cohort by sex and age

| Outcome | Hospital Cohort | Men | Women | p Value | Age <75 Yrs | Age \geq 75 Yrs | p Value |
|--|-------------------|-------------------|--------------------|---------|-----------------|--------------------|---------|
| | (n = 48,612) | (n = 23,537) | (n = 25,075) | | (n = 22,913) | (n = 25,612) | |
| In-hospital mortality* (%) | 3.7 | 3.9 | 3.6 | 0.026 | 2.4 | 4.9 | <0.001 |
| Median length of stay* (days), (IQR) | 4.0 (3.0, 7.0) | 4.0 (3.0, 7.0) | 4.0 (3.0, 7.0) | <0.001 | 4.0 (2.0, 7.0) | 4.0 (3.0, 7.0) | <0.001 |
| Mean length of stay* (days), (SD) | 5.7 (5.9) | 5.6 (6.1) | 5.7 (5.7) | <0.001 | 5.8 (6.7) | 5.6 (5.0) | <0.001 |
| | Follow-up Cohort | Men | Women | | Age <75 Yrs | Age \geq 75 Yrs | |
| | (n = 5,791) | (n = 2,965) | (n = 2,826) | | (n = 2,925) | (n = 2,854) | |
| 60–90-day Postdischarge mortality, (95% CI) [†] | 10.39 (9.3, 11.5) | 10.74 (9.2, 12.3) | 10.00 (8.4, 11.60) | 0.321 | 8.11 (6.7, 9.6) | 12.76 (11.1, 14.4) | <0.001 |
| 60–90-day Readmission | 29.6% | 29.8% | 29.4% | 0.777 | 29.8% | 29.4% | 0.709 |
| 60–90-day Mortality and/or rehospitalization | 36.2% | 36.2% | 36.2% | 0.990 | 34.5% | 38.1% | 0.005 |

CI = confidence interval; IQR = interquartile range.

* Patients dying beyond or with length of stay >120 days were censored.

[†] Event rate from Kaplan–Meier estimates.

characteristics are presented in Tables 1 and 2, stratified by gender and age <75 and \geq 75 years, respectively. Women represented most patients (58.6%) >75 years old in the OPTIMIZE-HF registry and were, on average, 4.6 years older than the participating men. Female patients were significantly less likely to have an ischemic etiology for their HF than were the men but were significantly more likely to have a history of hypertension. The mean left ventricular ejection fraction was significantly greater in women than in men, with 23% more women than men demonstrating HF with preserved left ventricular function. The left ventricular ejection fraction was significantly greater in older patients, and 14% more patients \geq 75 years old had HF with preserved left ventricular function compared with those <75 years old.

Figures 1 and 2 depict the implementation of evidence-based guideline recommendations at hospital discharge for eligible patients, by gender and age, respectively. Men and women were as likely to be discharged with ACE inhibitor/ARB for left ventricular systolic dysfunction or β blockers for left ventricular systolic dysfunction. However, fewer women than men were discharged with aldosterone antagonists for left ventricular systolic dysfunction or warfarin for atrial fibrillation. Notably, aldosterone antagonists were underprescribed to all groups studied. In addition, left ventricular function measurement ($p < 0.001$) and receipt of complete hospital discharge instructions were modestly less likely in the female cohort. All guideline-recommended cardiac medications were prescribed less frequently at discharge to patients \geq 75 years old than to those <75 years old

Table 5
Unadjusted and adjusted clinical outcomes in the hospital and follow-up cohort by female sex and older age

| | Women | | | | Age \geq 75 Yrs | | | |
|---|--|---------|--|---------|--|---------|--|---------|
| | Unadjusted | | Adjusted | | Unadjusted | | Adjusted | |
| | Odds, Hazard, or Length-of-Stay Ratio (95% CI) | p Value | Odds, Hazard, or Length-of-Stay Ratio (95% CI) | p Value | Odds, Hazard, or Length-of-Stay Ratio (95% CI) | p Value | Odds, Hazard, or Length-of-Stay Ratio (95% CI) | p Value |
| Hospital cohort | | | | | | | | |
| In-hospital mortality | 0.81* (0.74–0.89) | <0.001 | 0.95* (0.84–1.08) | 0.454 | 2.14* (1.93–2.36) | <0.001 | 1.76* (1.54–2.02) | <0.001 |
| Length of stay | 1.02 [†] (1.01–1.04) | <0.001 | 1.06 [†] (1.03–1.08) | <0.001 | 1.02 [†] (1.01–1.04) | <0.001 | 1.00 [†] (0.98–1.03) | 0.734 |
| Follow-up cohort | | | | | | | | |
| Postdischarge mortality | 0.85 [‡] (0.71–1.03) | 0.093 | 0.83 [‡] (0.68–1.02) | 0.069 | 1.77 [‡] (1.46–2.15) | <0.001 | 1.62 [‡] (1.26–2.08) | <0.001 |
| Postdischarge rehospitalization | 0.98* (0.88–1.10) | 0.801 | 0.96* (0.85–1.09) | 0.559 | 0.98* (0.88–1.10) | 0.733 | 0.95* (0.84–1.08) | 0.452 |
| Postdischarge mortality/rehospitalization | 0.98* (0.88–1.10) | 0.764 | 0.99* (0.89–1.10) | 0.828 | 1.17* (1.05–1.31) | 0.005 | 1.11* (0.96–1.28) | 0.147 |

Multivariate predictors of in-hospital mortality included age, heart rate, SBP, sodium, creatinine, HF as primary cause of hospitalization, and presence/absence of left ventricular systolic dysfunction; factors predicting early postdischarge mortality included age, serum creatinine, reactive airway disease, liver disease, lower SBP, lower serum sodium, lower admission weight, and depression.

* Odds ratio.

[†] Length-of-stay ratio.

[‡] Hazard ratio.

SBP = systolic blood pressure; other abbreviations as in Table 3.

(Figure 2). Furthermore, significantly fewer older patients underwent left ventricular function measurements, but the delivery of discharge instructions did not differ by age group. Overall, 7,345 patients (15%) had no left ventricular function assessment reported, most of whom were women (57%).

At the 60- to 90-day postdischarge follow-up visit, of those eligible, 60.9% of women and 64.7% of men were treated with ACE inhibitor/ARBs and 82.4% of women and 84.1% of men with β blockers (both $p = \text{NS}$). At follow-up, fewer patients ≥ 75 years old were treated with an ACE inhibitor/ARB (59.2% vs 66.1%) or β blockers (78.9% vs 86.5%) compared with those < 75 years old (both $p < 0.001$).

The independent effect of gender and age on evidence-based HF therapies was tested in multivariate models adjusted for patient and site characteristics, as well as for potential correlation of data within sites. For most quality measures, gender did not significantly influence the quality of care. Female gender was an independent predictor of a lower likelihood of receiving complete HF discharge instructions and evaluation of left ventricular systolic function (Table 3). Older age was independently associated with a lower likelihood of evaluation of left ventricular systolic function. In addition, the older age group was independently associated with a lower likelihood of prescriptions for a β blocker for left ventricular systolic dysfunction, aldosterone antagonist for left ventricular systolic dysfunction, or warfarin for atrial fibrillation on discharge.

The length of stay was similar for the men and women (Table 4). Male patients had a slightly greater unadjusted in-hospital mortality rate than female patients. The clinical outcomes after discharge were comparable in the men and women who were followed 60 to 90 days after hospital discharge (Table 4). Both groups experienced similarly high postdischarge mortality and readmission rates.

Older patients experienced poorer clinical outcomes (Table 4). The unadjusted in-hospital mortality of the ≥ 75 -year

age group was double that of the younger cohort. Older patients also died from any cause after discharge more frequently than did the younger patients. In addition, the occurrence of death and/or rehospitalization was greater in the older patients than in the younger patients (Table 4).

The effect of gender on in-hospital and follow-up outcomes was tested in risk-adjusted models. After adjustment for multiple variables predictive of outcome and for the correlation of data within hospitals, the length of stay for women was greater than that of men (Table 5). A gender difference was not found for other clinical outcomes, including rehospitalization, in-hospital mortality, and postdischarge mortality. Older age had an independent effect on mortality in both the in-hospital and follow-up cohorts (Table 5). Patients ≥ 75 years of age had a 76% increase in the risk of in-hospital mortality and a 62% increase in the risk of postdischarge mortality (Table 5). The occurrence of rehospitalization in the follow-up cohort did not differ by age group.

Discussion

HF greatly affects the elderly (median age 76 years), with men and women equally represented among patients hospitalized with HF.¹⁶ Despite female patients and older patients being at high risk of short-, intermediate-, and long-term morbidity and mortality from HF, previous studies have shown that women and older patients are less likely to be treated with guideline-recommended HF therapies than men and younger patients.^{3–6} Among hospitals participating in OPTIMIZE-HF, female patients with HF had better than previously observed treatment with guideline-recommended HF therapies. Furthermore, in adjusted analyses, gender did not influence hospital-based delivery of high-quality care, as indexed by most of the measures studied. In contrast, older patients with HF were less likely to

receive guideline-recommended HF care than younger patients.

Guideline-recommended HF therapies, including ACE inhibitors/ARBs and β blockers for left ventricular systolic dysfunction, are important components of modern HF care, yet they remain underused in a significant portion of suitable patients in conventional care settings.^{16,17} This may be because of physicians' lack of familiarity with their use, coupled with their concerns regarding the potential side effects.^{6,18,19} Two important population groups, in particular, that tend to be undertreated with these evidence-based HF therapies are women and older patients,^{3–6,20–25} although randomized clinical trial data have demonstrated mortality and morbidity benefits in these groups comparable to those of men and younger patients with HF, respectively.^{26,27} The American College of Cardiology and the American Heart Association HF guidelines give as a class I recommendation (level of evidence B) that groups of patients, including women and older patients, even if underrepresented in clinical trials, should, in the absence of specific evidence to direct otherwise, receive clinical screening and therapy in a manner identical to that applied to the broader HF population.²⁸ It is also specifically recommended that evidence-based therapy for HF be used in the elderly patient, with individualized consideration of the elderly patient's altered ability to metabolize or tolerate standard medications.²⁸ The results of the present study suggest that among hospitals participating in OPTIMIZE-HF the quality of care was similar for both men and women in some, but not all, guideline-recommended HF treatments. A lower rate of discharge prescriptions for certain guideline-recommended medications, including aldosterone antagonists for left ventricular systolic dysfunction and warfarin for atrial fibrillation, to women occurred. Female patients were still less likely to receive complete HF discharge instructions or to have had their left ventricular function measured. Previous studies in the usual care setting have consistently shown lower HF treatment rates for women. In a retrospective survey of 9,387 hospital admissions with HF from October 2005 to March 2006 in England, Wales, and Northern Ireland, gender-related disparities in care were reported. Women were significantly less likely to be prescribed HF medications on discharge compared with men (ACE inhibitor/ARB 66.5% vs 73.4%, β blocker 31.3% vs 37.5%, and aldosterone antagonists 23.4% vs 30.1%, all $p < 0.001$).²⁹ Although the goals of treatment of HF in the older population should be similar to those in younger patients, multiple studies have demonstrated much lower treatment rates with guideline-recommended therapies for elderly patients with HF compared with younger patients. A gap in the awareness of the beneficial effects of treatments such as ACE inhibitors, β blockers, and aldosterone receptor antagonists in elderly patients with HF could be an important reason these guideline-recommended therapies are not more frequently prescribed. Uncertainty may exist about the risks versus benefits in treating elderly patients who are underrepresented in randomized controlled trials. Misperceptions regarding contraindications and lack of tolerability in the elderly could also contribute to age-related treatment gaps and disparities in care. The increased difficulty experienced by older patients as they attempt to comply with the de-

mands of multiple medications, coupled with the desire to avoid side effects and adverse drug interactions, have also played an important role in limiting HF treatment to the elderly.⁶ These challenges make physicians more reluctant to initiate and up-titrate guideline-recommended therapies in elderly patients with HF.

In the present study, elderly patients were less likely to have their left ventricular function measured. They were also significantly less likely to be treated at discharge with all evidence-based therapies for left ventricular systolic dysfunction, including ACE inhibitors/ARBs, β blockers, or aldosterone antagonists. Previous studies have shown lower treatment rates in elderly patients with HF.^{5,6} Other studies have also reported similar findings in elderly patients with other cardiovascular conditions, including acute coronary syndromes, with lower rates of therapeutic intervention in elderly patients. Although the treatment rates in older patients with HF in OPTIMIZE-HF were lower than those achieved in younger patients, the absolute rate of treatment of patients aged ≥ 75 years are quite remarkable. With OPTIMIZE-HF, 78.8% of elderly patients with HF were successfully treated with ACE inhibitor/ARBs and 79.9% were successfully treated with β blockers at hospital discharge. In contrast, previous studies have shown much lower treatment rates with guideline-recommended therapies. The ACE inhibitor/ARB and β -blocker treatment rate at hospital discharge in eligible, higher risk, patients with HF in the Enhanced Feedback for Effective Cardiac Treatment (EFFECT) study was only 64% and 32%, respectively.³⁰

Gender-related differences in clinical outcomes were observed in the present study. The women's hospital length of stay was longer and the unadjusted in-hospital mortality was lower compared with men. The unadjusted and risk-adjusted clinical outcomes after discharge were, however, comparable in the male and female patients. In contrast, older patients had greater risk-adjusted mortality, both in-hospital and after discharge. Older age was independently associated with a 76% increase in in-hospital mortality risk and a 62% increase in postdischarge mortality risk. The substantially increased risk of mortality in older patients with HF has been observed in previous HF studies.³⁰ Failure to treat higher risk, elderly patients with HF with life-sustaining therapies could account in part for the adverse outcomes observed in this patient population.

Although OPTIMIZE-HF represents an opportunity to study patients with HF in a real-world setting, a registry-based study has several limitations. The data were collected by medical chart review and therefore were dependent on the accuracy and completeness of the documentation and abstraction. Because of the large number of patients in the registry, some small differences that might be of little clinical relevance had p values indicating a high degree of statistical significance. The 60- to 90-day follow-up data were only available for a subset of patients in the overall registry. Medication use was as reported by patients and as documented in the medical record. Contraindications and intolerance were as documented in the medical record, but a proportion of patients reported to be eligible for treatment but not treated might have had contraindications or intolerance that were present but not documented. Other aspects of the quality assessment such as the use of HF device therapy

and assessments of medications to avoid in HF were not included and should be assessed in future studies. The present study was not a prospective randomized trial; unmeasured confounders may have influenced the treatment rates and clinical outcomes. Additional research is needed to identify factors accounting for age-related gaps in HF care and to provide strategies to overcome them.

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