

Systolic Blood Pressure at Admission, Clinical Characteristics, and Outcomes in Patients Hospitalized With Acute Heart Failure

Mihai Gheorghiu, MD

William T. Abraham, MD

Nancy M. Albert, RN, PhD

Barry H. Greenberg, MD

Christopher M. O'Connor, MD

Lilin She, PhD

Wendy Gattis Stough, PharmD

Clyde W. Yancy, MD

James B. Young, MD

Gregg C. Fonarow, MD

for the OPTIMIZE-HF Investigators and Coordinators

ACUTE HEART FAILURE IS A MAJOR public health concern because of its prevalence and associated morbidity and mortality. In 2003, 1.1 million patients were discharged from the hospital for heart failure, making this the most common primary discharge diagnosis among patients older than 65 years.^{1,2} Until recently, the scientific community's understanding of acute heart failure syndromes (AHFS) had been based on demographic and outcome data obtained from randomized controlled trials.³ While these results drive therapeutic decision making, relying on clinical trial data to characterize the general acute heart failure population is limited by the fact that randomized controlled trials have tended to focus on a small proportion of AHFS patients. Because of selective enrollment criteria, clinical trials may

See also pp 2209 and 2259.

Context The association between systolic blood pressure (SBP) at admission, clinical characteristics, and outcomes in patients hospitalized for heart failure who have reduced or relatively preserved systolic function has not been well studied.

Objective To evaluate the relationship between SBP at admission, clinical profile, and outcomes in patients hospitalized for acute heart failure.

Design, Setting, and Patients Cohort study using data from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) registry and performance-improvement program for patients hospitalized with heart failure at 259 US hospitals between March 2003 and December 2004. Patients were divided into quartiles by SBP at hospital admission (<120, 120-139, 140-161, and >161 mm Hg). In-hospital outcomes were based on 48 612 patients aged 18 years or older with heart failure. Of the 41 267 patients with left ventricular function assessed, 21 149 (51%) had preserved left ventricular function. Postdischarge outcomes were based on a prespecified subgroup (n=5791, 10% of patients) with follow-up data assessed between 60 and 90 days.

Main Outcome Measures In-hospital and postdischarge mortality.

Results Patients with higher SBP were more likely to be female and black and to have preserved systolic function. Fifty percent of the patients had SBP higher than 140 mm Hg at admission. Patients with lower SBP at admission had higher in-hospital and postdischarge mortality rates. Higher SBP at admission was associated with lower in-hospital mortality rates: 7.2% (<120 mm Hg), 3.6% (120-139 mm Hg), 2.5% (140-161 mm Hg), and 1.7% (>161 mm Hg) ($P<.001$ for overall difference). Postdischarge mortality rates in the follow-up cohort by SBP at admission were 14.0%, 8.4%, 6.0%, and 5.4%, respectively ($P<.001$ for overall difference).

Conclusions Systolic hypertension is common in patients hospitalized for heart failure. Systolic blood pressure is an independent predictor of morbidity and mortality in patients with heart failure with either reduced or relatively preserved systolic function. Low SBP (<120 mm Hg) at hospital admission identifies patients who have a poor prognosis despite medical therapy. These findings may have important therapeutic implications because characteristics and outcomes differ greatly among patients with heart failure with varying SBP.

JAMA. 2006;296:2217-2226

www.jama.com

Author Affiliations: Division of Cardiology, Feinberg School of Medicine, Northwestern University, Chicago, Ill (Dr Gheorghiu); Division of Cardiology, Ohio State University, Columbus (Dr Abraham); George M. and Linda H. Kaufman Center for Heart Failure, Cleveland Clinic Foundation, Cleveland, Ohio (Drs Albert and Young); Department of Medicine, University of California San Diego Medical Center, San Diego (Dr Greenberg); Duke Clinical Research Institute, Durham, NC (Drs O'Connor and She); Department of Medicine, Duke University Medical Center, Durham, NC (Dr Stough); Campbell University School of

Pharmacy, Research Triangle Park, NC (Dr Stough); Department of Medicine, University of Texas Southwestern Medical Center, Dallas (Dr Yancy); and Department of Medicine, University of California Los Angeles Medical Center, Los Angeles (Dr Fonarow). Dr Yancy is now with the Baylor Heart and Vascular Institute, Baylor University Medical Center, Dallas, Tex. **Corresponding Author:** Gregg C. Fonarow, MD, Ahmanson-UCLA Cardiomyopathy Center, UCLA Medical Center, 10833 LeConte Ave, Room 47-123 CHS, Los Angeles, CA 90095 (gfonarow@mednet.ucla.edu).

not be representative of broad populations with AHFS.⁴ Registries can provide complementary data to clinical trials and may include patients that are a more representative sampling of the patient population of interest.

Based on the demographics of populations included in 6 recent acute heart failure clinical trials, the conclusion could be drawn that the majority of patients hospitalized for AHFS present with low or normal systolic blood pressure (SBP).⁵⁻¹¹ The mean SBP across these studies ranged from 106 to 132 mm Hg. However, data from the Acute Decompensated Heart Failure National Registry (ADHERE) revealed that the mean SBP at admission was higher (144 mm Hg) among an unselected patient population than that observed in randomized controlled trials.² Elevated SBP was common in ADHERE, with 50% of registry patients having admission values higher than 140 mm Hg.²

Elevated SBP may identify patients with certain clinical characteristics that are unique from those in patients with low SBP. Pathophysiological processes may also differ between these groups. Furthermore, patients with elevated SBP have been underrepresented in acute heart failure clinical trials. As a result, the relationship between SBP and clinical characteristics is not known.

In this study, the first report of outcomes from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) registry database, we evaluated the relationship between SBP at admission, clinical profile, and outcomes in patients hospitalized for acute heart failure.

METHODS

Data Collection and Hospitals

OPTIMIZE-HF was designed to evaluate the use of evidence-based, guideline-recommended therapy in patients hospitalized for heart failure and to improve the quality of care provided to these patients.¹² There were 2 components of the study: a Web-based data collec-

tion and reporting system and a process-of-care improvement program.

Data were collected by each site and entered into the electronic data capture system. Data were collected on patient demographics, medical history, signs, symptoms, medications, procedures, and outcomes, as previously described.¹² Systolic blood pressure at admission was defined as the supine measurement first obtained after presentation to the emergency department or, for patients directly admitted, what was first recorded on the medical ward. Admission staff, medical staff, or both recorded race/ethnicity, usually as the patient was registered. Prior studies in patients hospitalized with heart failure have suggested differences in characteristics and outcomes based on race/ethnicity.

Hospitals enrolled all consecutive patients meeting inclusion criteria or, if there were more than 75 hospitalizations per month, were given the option of using an electronic sampling tool that used a standard algorithm to generate a sample from an administrative file upload. Automated electronic data checks were used to prevent an "out-of-range entry" (eg, SBP value >300 mm Hg at admission), illogical data, or duplicate patients. A database audit was performed, based on predetermined criteria, of a random sample of 5% of the first 10 000 patients verified against source documents. The process-of-care improvement techniques consisted of real-time data reports on performance indicators and periodic educational programs. The registry data coordinating center was Outcome Sciences Inc (Cambridge, Mass). All statistical analyses were performed independently by Duke Clinical Research Institute, Durham, NC.

Patients and Outcomes

Patients aged 18 years or older with a discharge diagnosis of heart failure were eligible for enrollment. Patients with left ventricular systolic dysfunction (LVSD) and preserved systolic function were included. Patients were considered to have preserved systolic function if left

ventricular ejection fraction was documented as 40% or higher or if they were described as having left ventricular systolic function that was qualitatively normal or mildly impaired. Patients were considered to have LVSD if they had left ventricular ejection fraction of less than 40% or moderate to severe left ventricular dysfunction by qualitative assessment.

The incidence of death or rehospitalization within 60 to 90 days was prospectively collected on a prespecified 10% subset of the total OPTIMIZE-HF population. Sites had the option of participating in the collection of follow-up data. The protocol was approved by each participating center's institutional review board or through use of a central institutional review board. Written informed consent was obtained prior to enrollment from patients who participated during the follow-up period.

Statistical Analyses

Data are reported as mean (SD) for continuous variables or number (percentages) of patients for categorical variables. Admission SBP values were prospectively categorized into quartiles. Overall tests of any differences in patient characteristics and evidence-based treatments were compared using the Pearson χ^2 test for categorical variables and analysis of variance for continuous variables.

In-hospital mortality and the composite of postdischarge mortality or rehospitalization were analyzed using logistic regression modeling techniques. Analysis of variance was used for the length of stay analyses. To account for differential follow-up, Cox proportional hazards modeling was used for postdischarge mortality. The proportional hazards assumption was evaluated, and if a factor was found to be nonproportional it was included as a stratum.

Models had been previously developed to predict the risk of 4 outcomes of interest. These were used when performing adjusted models of these risks. Only baseline factors were used for the

2 in-hospital events (in-hospital mortality and length of stay). In addition, in-hospital treatments and events were included when modeling the 2 post-discharge outcomes. The variables for the 4 multivariable models include the following.

For the in-hospital mortality model, we included the following variables: age per 10-year increase, black race, heart rate per 10/min increase (range, 65-110/min), SBP per 10-mm Hg increase (≤ 160 mm Hg), diastolic blood pressure per 10-mm Hg increase (≤ 100 mm Hg), sodium level per 3-mEq/L decrease (≤ 140 mEq/L and > 140 mEq/L), serum creatinine level per 1-mg/dL increase (> 3.5 mg/dL [> 309.4 $\mu\text{mol/L}$]), hemoglobin level per 1-g/dL decrease (< 13 g/dL and ≥ 13 g/dL), primary cause of hospital admission, prior cerebrovascular accident or transient ischemic attack, hyperlipidemia, hypertension, liver disease, smoker within past year, chronic obstructive pulmonary disease, peripheral vascular disease, no known heart failure prior to this admission, rales, and LVSD.

For the length of stay model, we included the following variables: age per 10-year increase (< 80 years and ≥ 80 years), sex, weight per 10-kg increase, heart rate per 10/min increase (≥ 70 /min), SBP per 10-mm Hg increase (< 160 mm Hg), serum creatinine level per 1-mg/dL increase (< 3.5 mg/dL [< 309.4 $\mu\text{mol/L}$] and ≥ 3.5 mg/dL [≥ 309.4 $\mu\text{mol/L}$]), implantable cardiac defibrillator, sodium level per 3-mEq/L decrease (< 140 mEq/L and ≥ 140 mEq/L), hemoglobin level per 1-g/dL decrease (< 13 g/dL), primary cause of hospital admission, coronary artery disease or ischemic heart disease, renal disorder, atrial arrhythmia, prior cerebrovascular accident or transient ischemic attack, depression, diabetes (insulin dependent), hyperlipidemia, chronic obstructive pulmonary disease, pulmonary hypertension, peripheral vascular disease, ventricular arrhythmia, lower extremity edema, and LVSD.

For the postdischarge mortality model, we included the following vari-

Table 1. Patient Characteristics*

	Overall Registry (n = 48 612)	Follow-up Cohort (n = 5791)
Age, mean (SD), y	73.1 (14.2)	72.0 (14.1)
Male sex	23 537 (48)	2965 (51)
Black race	8608 (18)	1044 (18)
Ischemic etiology	22 219 (46)	2435 (42)
Hypertensive etiology	11 181 (23)	1827 (32)
LVSD†	20 118 (48.8)	2720 (53.2)
Left ventricular ejection fraction, mean (SD), %	39.0 (17.6)	36.9 (17.0)
No known prior heart failure	5675 (12)	697 (12)
Implantable cardioverter-defibrillator during hospitalization	975 (2)	187 (3)
Atrial fibrillation	14 970 (31)	1948 (34)
Medications prior to admission		
ACE inhibitor	19 273 (40)	2409 (42)
Aldosterone antagonist	3449 (7)	455 (8)
Amlodipine	3850 (8)	379 (7)
Angiotensin receptor blocker	5704 (12)	719 (12)
Antiarrhythmic	5035 (10)	720 (12)
Aspirin	19 217 (40)	2352 (41)
β -Blocker	25 800 (53)	3161 (55)
Digoxin	11 369 (23)	1417 (24)
Loop diuretic	29 683 (61)	3544 (61)
Hydralazine	1504 (3)	143 (2)
Statin‡	14 672 (39)	1872 (40)
Nitrate	10 499 (22)	1276 (22)
Intravenous medications during hospitalization		
Any inotrope	3564 (7)	414 (7)
Nesiritide	5225 (11)	597 (10)
Other intravenous vasodilator	1650 (3)	170 (3)
Weight change from admission to discharge, mean (SD), kg	-2.6 (9.1)	-2.6 (8.6)
B-type natriuretic peptide, mean (SD), pg/mL	1272.91 (1330.07)	1290.65 (1295.32)
Creatinine level, mean (SD), mg/dL		
At admission	1.8 (1.8)	1.7 (1.4)
At discharge	1.8 (1.4)	1.7 (1.2)
Systolic blood pressure, mean (SD), mm Hg		
Overall at admission	142.6 (33.2)	140.3 (32.8)
At admission in patients with LVSD	135.2 (30.9)	133.2 (30.1)
At discharge	124.3 (24.0)	122.5 (25.2)
Change from admission to discharge	-18.4 (30.6)	-17.1 (29.7)
Edema		
At admission	30 710 (65)	3686 (65)
At discharge	10 395 (27)	1209 (24)
Rales		
At admission	30 546 (64)	3522 (62)
At discharge	6292 (15)	658 (13)
Dyspnea at admission		
On exertion	29 856 (61)	3670 (63)
At rest	21 279 (44)	2559 (44)
Heart rate, mean (SD), beats/min		
At admission	87 (21.5)	86 (21.3)
At discharge	75.9 (15.0)	75.8 (14.5)
Sodium, mean (SD), mEq/L	136.7 (11.0)	136.8 (9.2)
Hemoglobin, mean (SD), g/dL	12.1 (3.4)	12.2 (2.3)
Orthopnea at admission	13 298 (27)	2051 (35)
Paroxysmal nocturnal dyspnea at admission	7338 (15)	1277 (22)

Abbreviations: ACE, angiotensin-converting enzyme; LVSD, left ventricular systolic dysfunction.

SI conversion factor: To convert creatinine to $\mu\text{mol/L}$, multiply by 88.4.

*Values are expressed as number (percentage) unless otherwise indicated.

†The number (percentage) of those with LVSD assessed. Defined as left ventricular ejection fraction of less than 40% or moderate to severe LVSD.

‡Statin use in patients with medical history of coronary artery disease, cerebrovascular accident or transient ischemic attack, diabetes, hyperlipidemia, or peripheral vascular disease.

Table 2. Hospital Characteristics

	No. (%) of Hospitals	
	Total (n = 259)	Follow-up (n = 91)
Bed size		
0-99	31 (12)	9 (10)
100-249	58 (22)	21 (23)
250-499	103 (40)	40 (44)
500-749	38 (15)	13 (14)
≥750	13 (5)	4 (4)
Unknown	16 (6)	4 (4)
Academic	118 (48)	48 (55)
Transplant program	34 (14)	9 (10)
Interventional (CABG surgery/PCI)	163 (67)	62 (70)
Region		
Midwest	68 (27)	27 (30)
Northeast	44 (17)	14 (16)
South	87 (34)	34 (38)
West	56 (22)	15 (17)

Abbreviations: CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

ables: SBP per 10-mm Hg increase (<140 mm Hg and ≥140 mm Hg) at admission, serum creatinine level lower than 4 mg/dL per unit increase (<4 mg/dL [$<353.6 \mu\text{mol/L}$]) at admission, age per 10-year increase, reactive airway disease, weight per 10-kg increase, lower extremity edema, lipid-lowering agent at discharge, sodium level per 1-mEq/L increase (<140 mEq/L), depression, any β -blocker use at discharge, SBP per 10-mm Hg increase (<130 mm Hg) at discharge, serum creatinine level per 1-mg/dL increase (<3 mg/dL [$<265.2 \mu\text{mol/L}$]) at discharge, and liver disease.

For the postdischarge mortality and rehospitalization model, we included the following variables: hemoglobin level at admission (all levels <11 have equal risk), serum creatinine level at admission ($\leq 3.8 \text{ mg/dL}$ [$\leq 335.9 \mu\text{mol/L}$]), diuretic use at admission, chronic obstructive pulmonary disease, heart failure hospitalization in past 6 mo (yes/no), nitrate use at admission, digoxin use at admission, prior cerebrovascular accident or transient ischemic attack, SBP per increments of 10 mm Hg, coronary angiography performed during hospitalization, angiotensin receptor blocker use at discharge, mechanical ventilation performed during hospitalization, angiotensin-converting enzyme inhibitor use at discharge, implantable cardiac defibrillator placed

during hospitalization, and lipid-lowering agent use at discharge.

For each of the 4 outcomes, a similar modeling process was used. The assumption of linearity was evaluated for the continuous measures using restricted cubic splines and when violated appropriate transformations were applied. Both forward stepwise and backward variable selection techniques were applied to the data with a value of .05 for both inclusion and remaining in the model. The forward stepwise selection process was also bootstrapped using 200 samples. The final factors for a model must have been selected by at least 1 of the 2 selection methods and at least 50% of the bootstrapped samples.

If SBP was not selected as 1 of the covariates in the model, it was included to evaluate the association of this factor with outcome after adjusting for potential confounders. The *c* statistic was 0.77 for the in-hospital model and 0.74 for the postdischarge model. For all statistical analyses, SAS software version 8.2 (SAS Institute Inc, Cary, NC) was used. With the large sample size of the hospital cohort, one would expect statistical significances with small differences. No adjustment has been made for multiple comparisons, which should be considered in the interpretation of the *P* values.

RESULTS

OPTIMIZE-HF enrolled 48 612 patients (TABLE 1) between March 2003 and December 2004 from 259 hospitals across the United States. Academic and community-based centers of all sizes and from all regions of the country were represented (TABLE 2).

The mean age of the overall cohort was 73 years; 52% were women and 74% were white. Of the 48 612 patients, 41 267 (84.9%) had data for left ventricular ejection fraction or a qualitative assessment of left ventricular function. Of the patients with left ventricular function assessed, 20 118 (49%) had LVSD and 21 149 (51.2%) had heart failure with preserved systolic function. Systolic blood pressure at ad-

mission was missing in 45 (0.1%) of 48 612 patients.

At the 91 hospitals in the follow-up cohort, there were 19 082 potential patients for follow-up, of whom 6121 provided informed consent and were enrolled. Of these patients, follow-up data was unavailable for 330, resulting in 5791 patients in the follow-up population. The characteristics of the follow-up cohort were similar to the overall hospital cohort (Table 1).

The mean (SD) SBP at admission in the total cohort was 143 (33) mm Hg. Fifty percent of the patients had SBP at admission that was higher than 140 mm Hg. Systolic blood pressure at admission was higher than 140 mm Hg in 38% of the patients with LVSD and in 56% of patients without LVSD. Patients were categorized into quartiles based on their admission SBP values (TABLE 3). Quartile 1 included 12 252 patients with SBP below 120 mm Hg; quartile 2, 12 096 patients with SBP in the range of 120 to 139 mm Hg; quartile 3, 12 099 patients with SBP in the range of 140 to 161 mm Hg; and quartile 4, 12 120 patients with SBP higher than 161 mm Hg.

Patient characteristics differed across admission SBP quartiles (Table 3). Specifically, more patients in the higher SBP quartiles (140-161 mm Hg and >161 mm Hg) had preserved systolic function. A higher proportion of patients in the higher admission SBP quartiles were black. Other statistically significant differences were observed that may or may not be of clinical relevance because of the large numbers of patients (Table 3). For instance, a larger proportion of patients were classified as having new-onset heart failure in the higher SBP quartiles. The mean change in SBP from admission to discharge was different in each quartile, although all changes were statistically significant. In the quartile with the lowest SBP values at admission (<120 mm Hg), there was a mean increase of approximately 6.5 mm Hg from admission to discharge. In the next 3 quartiles, mean SBP was reduced from admission to discharge: quartile 2, -8.7; quartile 3, -21.3; quartile 4, -49.2.

Table 3. Demographics by Systolic Blood Pressure at Admission*

	Systolic Blood Pressure Quartile, mm Hg			
	<120 (n = 12 252)	120-139 (n = 12 096)	140-161 (n = 12 099)	>161 (n = 12 120)
Age, mean (SD), y	72.9 (14)	74 (13.5)	73.8 (13.6)	72.1 (14.6)
Female sex	5314 (43.4)	5941 (49.1)	6683 (55.2)	7112 (58.7)
Black race	1525 (12.4)	1688 (14.0)	2279 (18.8)	3111 (25.7)
Left ventricular systolic dysfunction†	6612 (62.8)	5367 (52.2)	4530 (44.1)	3585 (35.3)
Left ventricular ejection fraction, mean (SD), %	33.3 (17.4)	37.8 (17.6)	40.9 (17.1)	44.4 (16.5)
Ischemic etiology	6210 (50.7)	5903 (48.8)	5332 (44.1)	4753 (39.2)
Hypertensive etiology	1645 (13.4)	2190 (18.1)	3071 (25.4)	4216 (34.8)
No known prior heart failure	1034 (8.4)	1334 (11)	1565 (12.9)	1742 (14.4)
Atrial arrhythmia	4365 (35.6)	4099 (33.9)	3692 (30.5)	2798 (23.1)
Implantable cardioverter-defibrillator during hospitalization	1140 (9.3)	630 (5.2)	436 (3.6)	276 (2.3)
Medications prior to admission				
ACE inhibitor	5021 (41.0)	4677 (38.7)	4668 (38.6)	4897 (40.4)
Aldosterone antagonist	1448 (11.8)	955 (7.9)	630 (5.2)	413 (3.4)
Amlodipine	503 (4.1)	862 (7.1)	1110 (9.2)	1374 (11.3)
Angiotensin receptor blocker	1275 (10.4)	1309 (10.8)	1403 (11.6)	1713 (14.1)
Antiarrhythmic	1714 (14.0)	1312 (10.8)	1106 (9.1)	899 (7.4)
Aspirin	4909 (40.1)	4801 (39.7)	4841 (40.0)	4649 (38.4)
β-Blocker	6624 (54.1)	6197 (51.2)	6318 (52.2)	6634 (54.7)
Digoxin	3710 (30.3)	3019 (25.0)	2585 (21.4)	2041 (16.8)
Loop diuretic	8536 (69.7)	7639 (63.2)	7184 (59.4)	6294 (51.9)
Hydralazine	274 (2.2)	311 (2.6)	376 (3.1)	541 (4.5)
Statin	3871 (31.6)	3876 (32.0)	3868 (32.0)	3806 (31.4)
Nitrate	2527 (20.6)	2635 (21.8)	2662 (22.0)	2668 (22.0)
Intravenous medications during hospitalization				
Any inotrope	1838 (15.0)	786 (6.5)	549 (4.5)	384 (3.2)
Nesiritide	1571 (12.8)	1315 (10.9)	1197 (9.9)	1137 (9.4)
Other intravenous vasodilator	263 (2.1)	301 (2.5)	375 (3.1)	709 (5.8)
Creatinine, mean (SD), mg/dL				
At admission	1.8 (1.2)	1.6 (1.2)	1.7 (1.5)	2.0 (2.1)
At discharge	1.6 (1.1)	1.6 (1.1)	1.7 (1.5)	2.0 (2.1)
B-type natriuretic peptide, mean (SD), pg/mL	1416 (1429)	1229 (1289)	1197 (1268)	1271 (1316)
Weight change from admission to discharge, mean (SD), kg	-2.5 (5)	-2.7 (4.8)	-2.6 (4.6)	-2.4 (4.6)
Systolic blood pressure, mean (SD), mm Hg				
At admission	105 (11)	129 (6)	150 (6)	187 (22)
Left ventricular systolic dysfunction	(n = 6612) 104 (11)	(n = 5367) 129 (6)	(n = 4530) 149 (6)	(n = 3585) 185 (20)
At discharge	112 (19)	121 (19)	128 (20)	138 (23)
Change from admission to discharge	6.5 (19.9)	-8.7 (19.3)	-21.3 (20.6)	-49.2 (28.5)
Diastolic blood pressure, mean (SD), mm Hg				
At admission	62 (12)	72 (13)	79 (15)	92 (20)
At discharge	63 (11)	66 (12)	68 (13)	71 (14)
Change from admission to discharge	0.45 (14.7)	-6.1 (15.3)	-11.4 (16.8)	-22.4 (20.8)
Heart rate, mean (SD), beats/min				
At admission	85 (21)	86 (21)	86 (21)	90 (22)
At discharge	78 (15)	77 (14)	75 (14)	74 (13)
Edema				
At admission	7630 (63.9)	7708 (65.1)	7769 (65.6)	7588 (63.9)
At discharge	2817 (30.1)	2610 (27.1)	2637 (27.0)	2329 (23.8)
Rales				
At admission	7207 (60.3)	7450 (62.8)	7755 (65.2)	8116 (67.9)
At discharge	1794 (18.2)	1552 (15.3)	1554 (15.1)	1389 (13.4)
Dyspnea at admission				
At rest	5259 (42.9)	5261 (43.5)	5238 (43.3)	5485 (45.3)
On exertion	7294 (59.5)	7377 (61.0)	7508 (62.1)	7642 (63.1)
Orthopnea at admission	3089 (25.2)	3293 (27.2)	3376 (27.9)	3538 (29.2)
Paroxysmal nocturnal dyspnea at admission	1726 (14.1)	1782 (14.7)	1882 (15.6)	1945 (16.0)

Abbreviation: ACE, angiotensin-converting enzyme.

SI conversion factor: To convert creatinine to μmol/L, multiply by 88.4.

*Values are expressed as number (percentage) unless otherwise indicated.

†Defined as left ventricular ejection fraction of less than 40% or moderate to severe left ventricular dysfunction.

Parenteral inotropes or vasodilators were used more often for patients in the lower SBP quartiles. The use of any ino- trope decreased from 15% in the low- est SBP quartile to 3% in the highest SBP quartile ($P<.001$). Nesiritide use also decreased with increasing SBP but to a lesser extent. Nesiritide was pre- scribed in 12.8% of patients in the low-

Table 4. Clinical Event Rates by Systolic Blood Pressure at Admission and Left Ventricular Systolic Dysfunction*

	Systolic Blood Pressure Quartile, mm Hg				P Value Across Quartiles
	<120	120-139	140-161	>161	
Overall cohort (n = 48 612)†	(n = 12 252)	(n = 12 096)	(n = 12 099)	(n = 12 120)	
In-hospital mortality	7.2 (6.7-7.6)	3.6 (3.3-4.0)	2.5 (2.2-2.7)	1.7 (1.5-2.0)	<.001
Length of stay, mean (95% CI), d	6.5 (6.4-6.6)	5.7 (5.6-5.8)	5.4 (5.3-5.5)	5.1 (5.0-5.2)	<.001
Follow-up cohort (n = 5791)‡	(n = 1557)	(n = 1469)	(n = 1429)	(n = 1325)	
Postdischarge mortality	14.0 (12.2-15.7)	8.4 (7.0-9.8)	6.0 (4.7-7.2)	5.4 (4.2-6.7)	<.001
Rehospitalization for 60-90 d	30.6 (28.3-32.9)	29.9 (27.5-32.2)	30.3 (27.9-32.7)	27.6 (25.2-30.0)	.31
Subgroup with left ventricular function measured (n = 41 267)§	(n = 10 525)	(n = 10 276)	(n = 10 263)	(n = 10 161)	
In-hospital mortality	6.5 (6.0-6.9)	3.2 (2.8-3.5)	2.2 (2.0-2.5)	1.5 (1.2-1.7)	<.001
Length of stay, mean (95% CI), d	6.7 (6.6-6.8)	5.9 (5.8-6.0)	5.6 (5.5-5.7)	5.2 (5.1-5.3)	<.001
Follow-up cohort with left ventricular function measured (n = 4959)‡	(n = 1336)	(n = 1259)	(n = 1240)	(n = 1113)	
Postdischarge mortality	13.6 (11.8-15.5)	8.2 (6.7-9.7)	5.5 (4.2-6.8)	4.5 (3.3-5.7)	<.001
Rehospitalization for 60-90 d	30.6 (28.2-33.1)	29.9 (27.4-32.4)	30.3 (27.8-32.9)	27.2 (24.6-29.8)	.23
Patients with left ventricular systolic dysfunction (n = 20 118)	(n = 6612)	(n = 5367)	(n = 4530)	(n = 3585)	
In-hospital mortality	6.6 (6.0-7.2)	3.1 (2.6-3.6)	2.5 (2.1-3.0)	1.6 (1.2-2.0)	<.001
Length of stay, mean (95% CI), d	6.8 (6.6-6.9)	5.8 (5.8-5.9)	5.6 (5.4-5.7)	5.1 (4.9-5.1)	<.001
Postdischarge mortality	13.0 (10.8-15.2)	6.8 (5.0-8.7)	6.3 (4.4-8.2)	4.1 (2.2-6.0)	<.001
Rehospitalization for 60-90 d	31.5 (28.5-34.5)	28.6 (25.4-31.9)	32.4 (28.7-36.1)	25.5 (21.3-29.6)	.15
No left ventricular systolic dysfunction (n = 21 149)¶	(n = 3913)	(n = 4909)	(n = 5733)	(n = 6576)	
In-hospital mortality	6.2 (5.4-6.9)	3.2 (2.7-3.7)	2.0 (1.6-2.4)	1.4 (1.1-1.7)	<.001
Length of stay, mean (95% CI), d	6.5 (6.3-6.6)	5.9 (5.7-6.0)	5.5 (5.4-5.7)	5.3 (5.2-5.4)	<.001
Postdischarge mortality	14.9 (11.6-18.2)	10.0 (7.4-12.5)	4.7 (3.1-6.4)	4.7 (3.2-6.3)	<.001
Rehospitalization for 60-90 d	29 (24.9-33.1)	31.6 (27.8-35.5)	28.4 (25.0-31.9)	28.2 (24.9-31.5)	.44

Abbreviation: CI, confidence interval.
 *Values are expressed as percentage (95% CI) unless otherwise indicated.
 †Systolic blood pressure at admission was missing in 45 patients.
 ‡Systolic blood pressure at admission was missing in 11 patients.
 §Systolic blood pressure at admission was missing in 42 patients.
 ||Systolic blood pressure at admission was missing in 24 patients.
 ¶Systolic blood pressure at admission was missing in 18 patients.

Table 5. In-Hospital Mortality Risk by Systolic Blood Pressure Quartiles in Patients Receiving Parenteral Inotropic Agents, Vasodilators, or Neither*

	Systolic Blood Pressure Quartile, mm Hg				P Value Across Quartiles
	<120	120-139	140-161	>161	
Overall cohort, No. of hospital deaths/ No. of patients in SBP quartile (N=48 612)	(n = 12 252)	(n = 12 096)	(n = 12 099)	(n = 12 120)	
In-hospital death	881/12 252	441/12 096	297/12 099	209/12 120	
In-hospital death	7.2 (6.7-7.6)	3.6 (3.3-4.0)	2.5 (2.2-2.7)	1.7 (1.5-2.0)	<.001
Patients with no parenteral therapies, No. of hospital deaths/No. of patients in SBP quartile (n = 39 401)	490/9058	306/9959	186/10 226	138/10 126	
In-hospital death	5.4 (4.9-5.9)	3.1 (2.7-3.4)	1.8 (1.6-2.1)	1.4 (1.1-1.6)	<.001
Patients with inotropes, No. of hospital deaths/ No. of patients in SBP quartile (n = 2620)‡‡	252/1404	64/569	45/375	26/265	
In-hospital death	17.9 (15.9-20.0)	11.2 (8.7-13.8)	12.0 (8.7-15.3)	9.8 (6.2-13.4)	<.001
Patients with vasodilators, No. of hospital deaths/ No. of patients in SBP quartile (n = 5647)‡§	60/1356	36/1351	40/1324	33/1610	
In-hospital death	4.4 (3.3-5.5)	2.7 (1.8-3.5)	3.0 (2.1-3.9)	2.0 (1.4-2.7)	.002

Abbreviation: SBP, systolic blood pressure.
 *Values are expressed as percentage (95% confidence interval) unless otherwise indicated. Systolic blood pressure at admission was missing in 45 (0.1%) of 48 612 patients.
 †Inotropes indicate dobutamine, milrinone, and dopamine.
 ‡Patients with both inotropes and vasodilators are excluded.
 §Vasodilators indicate nesiritide or other intravenous vasodilator.

est SBP quartile and 9.4% in the highest SBP quartile ($P < .001$). Other intravenous vasodilators were used more often in the higher SBP quartiles (2.1% in the lowest vs 5.8% in the highest quartile; $P < .001$). Overall, diuretic use at admission was highest (73.3%) in patients in the lowest SBP quartile and much lower (57.4%) in patients in the highest SBP quartile ($P < .001$).

The in-hospital mortality rate was 3.8% in the entire cohort and the mean length of stay was 6.4 days. Higher SBP at admission was associated with substantially lower in-hospital mortality: 7.2% (<120 mm Hg), 3.6% (120-139 mm Hg), 2.5% (140-161 mm Hg), and 1.7% (>161 mm Hg) ($P < .001$ for overall difference; c statistic=0.65; TABLE 4). Lower SBP (<120 mm Hg) at admission was associated with higher in-hospital mortality risk in patients receiving parenteral inotropic agents, vasodilators, or neither (TABLE 5).

In the follow-up cohort, higher SBP at admission was also associated with lower 60- to 90-day mortality (c statistic=0.61) (Table 4). While higher admission SBP was associated with shorter length of stay ($r=0.01$), rehospitalization rates during follow-up were similar regardless of SBP at admission: 30.6% (<120 mm Hg), 29.9% (120-139 mm Hg), 30.3% (140-161 mm Hg), and 27.6% (>161 mm Hg) ($P = .31$). The as-

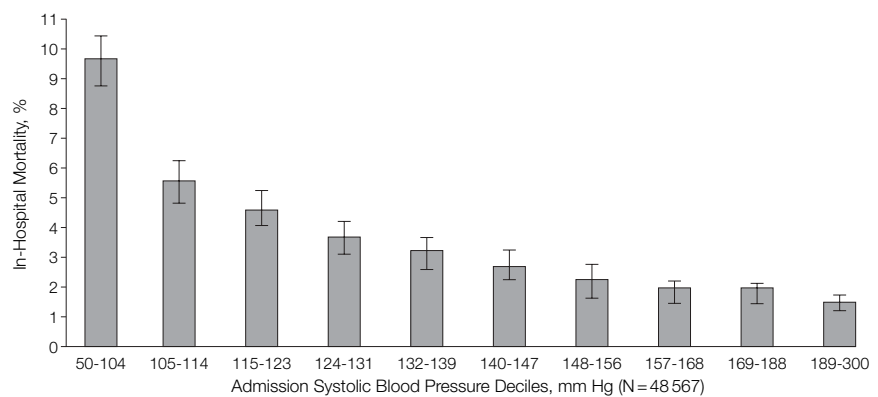
sociation between SBP and clinical events was not statistically significantly different among patients with and without systolic dysfunction (Table 4).

A monotonic relationship was observed when the association between SBP at admission and in-hospital mortality was examined further by SBP deciles and restricted cubic splines, with no suggestion of increased mortality even with extremely high SBP at admission (FIGURE).

Admission SBP was a significant predictor of in-hospital and postdischarge mortality after adjusting for other factors. The odds of in-hospital death increased 21% for each 10-mm Hg decrease in SBP below 160

mm Hg (odds ratio, 1.21; 95% confidence interval [CI], 1.17-1.25). The in-hospital mortality risk did not change for SBP above 160 mm Hg. Admission SBP also independently predicted postdischarge mortality, with an 18% increase in hazard ratio for each 10-mm Hg decrease in SBP (hazard ratio, 1.18; 95% CI, 1.10-1.26). For SBP above 140 mm Hg, the increase in risk with each 10-mm Hg decrease in SBP was 8%, which was statistically significant (hazard ratio, 1.08; 95% CI, 1.01-1.15). Across all values of SBP, the odds for the composite of mortality and rehospitalization increased 5% with each 10-mm Hg decrease in SBP (odds ratio, 1.05; 95% CI, 1.03-1.07). Inclu-

Figure. In-Hospital Mortality Rates by Admission Systolic Blood Pressure Deciles (n = 48 567)



$P < .001$ for trend across deciles. Error bars indicate 95% confidence intervals.

Table 6. Performance Measures at Discharge by Systolic Blood Pressure at Admission

	Systolic Blood Pressure Quartile, mm Hg % (95% Confidence Interval)				P Value Across Quartiles
	<120 (n = 10 525)	120-139 (n = 10 276)	140-161 (n = 10 263)	>161 (n = 10 161)	
At discharge					
Instructions	57.0 (55.9-58.2)	54.9 (53.8-56.0)	53.6 (52.5-54.6)	50.2 (49.2-51.2)	<.001
Left ventricular function assessment	87.7 (87.0-88.3)	86.7 (86.1-87.4)	86.2 (85.5-86.8)	85.5 (84.9-86.2)	<.001
ACE inhibitor	73.0 (71.7-74.4)	75.3 (74.0-76.7)	76.1 (74.7-77.5)	77.8 (76.3-79.4)	<.001
ACE inhibitor or ARB	79.9 (78.7-81.1)	82.2 (81.0-83.4)	84.0 (82.8-85.2)	85.8 (84.5-87.1)	<.001
Smoking cessation counseling	63.4 (61.0-65.8)	63.5 (61.1-65.8)	62.3 (59.9-64.7)	61.2 (59.0-63.4)	.46
β-Blocker	81.6 (80.5-82.7)	82.7 (81.6-83.9)	84.0 (82.9-85.2)	85.0 (83.7-86.2)	<.001
Warfarin in atrial fibrillation	55.0 (53.4-56.7)	53.1 (51.5-54.8)	53.1 (51.4-54.9)	46.3 (44.4-48.3)	<.001
Statin*	36.5 (35.5-37.5)	39.0 (38.1-40.0)	39.9 (38.9-40.9)	41.2 (40.2-42.1)	<.001
Aldosterone antagonist†	20.6 (19.6-21.5)	18.1 (17.1-19.1)	17.1 (16.0-18.2)	14.4 (13.2-15.5)	<.001

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

*Use among patients with coronary artery disease, cerebrovascular disease or transient ischemic attack, diabetes, hyperlipidemia, or peripheral vascular disease.

†Use among patients with left ventricular systolic dysfunction.

sion of intravenous medications during hospitalizations and discharge oral medications in the multivariable models for postdischarge mortality showed that admission SBP was still a significant predictor of mortality at 60 to 90 days, independent of medications and other variables.

The association between SBP at admission and performance indicators and the use of evidence-based therapies are shown in TABLE 6. Associations were observed between admission SBP and several performance indicators as well as the use of evidence-based therapies.

COMMENT

The OPTIMIZE-HF data provide insight into the characteristics of a broad population of patients with acute heart failure. These results provide evidence that elevated SBP is common in patients hospitalized for ADHS, including patients with reduced systolic function. These data are consistent with the findings from other registries such as ADHERE and Enhanced Feedback for Effective Cardiac Treatment (EFFECT).^{2,13} However, these observations are in contrast with data from clinical trials that suggest patients hospitalized with AHFS are most commonly admitted with low or normal SBP.

Furthermore, this analysis demonstrates that SBP at hospital admission, a readily accessible vital sign, is an important and independent predictor of morbidity and mortality in patients with heart failure, including patients with reduced or relatively preserved systolic function. Systolic blood pressure at hospital admission can effectively identify groups of patients that differ with respect to clinical characteristics, prognosis, and perhaps underlying pathophysiology. Accordingly, the therapeutic approach may vary among patients with high, normal, or low SBP.

Several notable differences were observed in patient characteristics across SBP quartiles. For example, the proportion of women within each quartile increased as SBP increased. The proportion of black patients was also

greater in the higher SBP quartiles. A lower proportion of patients had an ischemic etiology in the higher SBP quartiles. Left ventricular systolic dysfunction was more prevalent in the lower SBP quartiles. These observations are consistent with the existing data that hypertension is most prevalent in women and blacks, and is more often associated with preserved systolic function.¹⁴⁻¹⁶

Patients with elevated SBP at hospital admission may have a better response to in-hospital treatments for acute heart failure. At admission, congestive symptoms were more common in the higher SBP quartiles. However, by the time of discharge, these symptoms were less common in the higher SBP quartiles and more common in the lower SBP quartiles. In addition, elevated SBP did not appear to persist for the duration of the hospitalization. By the time of discharge, the overall mean SBP decreased from baseline. Systolic blood pressure also decreased from baseline within quartiles 2, 3, and 4, and increased from baseline within quartile 1. These observations suggest that patients with elevated SBP tended to respond to treatments administered during hospitalization from the standpoint of symptom resolution and reduction in SBP.

Elevated SBP also signaled a group of patients who were prognostically different from those with lower SBP. Higher SBP was associated with better in-hospital and short-term (60-90 days) survival. Even patients with extremely high (188-300 mm Hg) SBP at admission had a low risk for in-hospital mortality. Patients with SBP below 120 mm Hg at admission were at particularly high risk with a combined in-hospital and early postdischarge mortality risk of 21.2%. However, even among normotensive patients (SBP of 120-139 mm Hg), the combined in-hospital and postdischarge mortality was substantial at 12%. These patients were treated with angiotensin-converting enzyme inhibitors and β -blockers, but this mortality rate per-

sisted. This observation emphasizes the need to implement other evidence-based strategies in an effort to reduce mortality.

The finding that SBP was a significant predictor of outcome is consistent with other studies that have demonstrated the prognostic importance of SBP.¹⁷⁻²⁰ These studies have reported adjusted relative risks for mortality ranging from 0.78 to 0.90 for each 10-mm Hg increase in SBP.^{17,18,20} The association between SBP and mortality in OPTIMIZE-HF was similar, with an adjusted relative in-hospital mortality risk of 0.83 for each 10-mm Hg increase in SBP up to 160 mm Hg and an adjusted follow-up mortality risk of 0.85 for each 10-mm Hg increase in SBP up to 140 mm Hg. Short-term readmission rates were high regardless of SBP. Thus, patients with an elevated SBP at admission are at high risk of subsequent morbid events even though they appear to have a much lower short-term mortality risk. Physicians may perceive that a patient with normal or borderline-high SBP and heart failure is less severely ill than a hypotensive patient with heart failure. While this supposition may be accurate with regard to mortality, it does not appear to be true for morbid events. Physicians should recognize that these patients are at high risk of rehospitalization and should aggressively manage their disease in an effort to reduce recurrent hospitalizations.

This analysis focused on SBP because previous studies found less of a relationship between diastolic blood pressure and outcomes in patients with acute heart failure.¹⁹ Diastolic blood pressure at admission was included in the in-hospital mortality model but it was less predictive of mortality than SBP. More importantly, SBP at admission was predictive of outcome independently of diastolic blood pressure.

The findings from this analysis may provide insight into the pathophysiological processes that occur in AHFS. It has been hypothesized that the elevated SBP at admission observed in the majority of AHFS patients may be related to neurohormonal and cytokine

activation resulting in increased afterload.³ Patients with this clinical presentation may be those with early or mid-stage disease. The pathophysiology may differ in patients presenting with low SBP, who may be more likely to have advanced or end-stage disease with low cardiac output and signs of organ hypoperfusion.³ Systolic blood pressure may be a marker for a different stage of the disease or for a different pathophysiology altogether.

Recognizing SBP as a signal of the underlying pathophysiological process has important implications for future studies investigating treatment approaches. These data from OPTIMIZE-HF demonstrate that clinical characteristics and outcomes differ substantially between patients with higher and lower SBP. These groups could potentially be viewed as 2 unique populations. Thus, clinical trials should be designed to limit enrollment to only 1 patient type based on SBP or should stratify enrollment by SBP at admission.

It is reasonable to hypothesize that patients with elevated SBP may respond favorably to vasodilators and neurohormonal antagonists. However, these patients have typically been underrepresented in clinical trials, and as a result it is not possible to determine whether they benefit from these agents. None of the agents (vasodilators, inodilators, and calcium sensitizers) studied in recent trials⁵⁻¹¹ has improved clinical outcomes. The hypotensive effects of these drugs may potentially explain the lack of benefit or potential harm observed in these studies. Additional lowering of SBP in a patient with baseline hypotension may result in organ hypoperfusion, worsening renal function, cardiac ischemia, and reductions in cardiac output.

Our findings revealed that inotropes and nesiritide were used more commonly in patients with lower SBP, however these agents should be used with caution in patients with lower SBP. Patients with elevated SBP may respond to acute heart failure treatments differently, and they may be more likely to benefit from vasodilators or

acute neurohormonal antagonists than patients with low SBP. This hypothesis needs further investigation in randomized controlled trials.

The observed differences in performance measures and evidence-based medicine prescribing were interesting. Higher angiotensin receptor blocker, angiotensin-converting enzyme inhibitor, and β -blocker use in the higher SBP quartiles may be related to their antihypertensive effects. It is possible that poor outcomes associated with lower SBP may be due to reluctance on the part of the physician to use 1 or more of these therapies in patients with low SBP. The finding that therapies proven to reduce morbidity and mortality, such as angiotensin-converting enzyme inhibitors and β -blockers, were used more frequently in patients with higher SBP may indicate that physicians are more willing to treat patients with higher SBP—those who they may consider to be less sick—more aggressively. It is also possible that the use of higher doses of heart failure medications may have influenced the better outcomes observed in patients with higher SBP.

Lower rates of aldosterone antagonist use and lower rates of adherence to the discharge instructions and left ventricular ejection fraction assessment performance measures may be related to a perception that patients with normal or elevated SBP are less ill or at lower risk than those with hypotension and do not need to be treated aggressively. Although patients with higher SBP did have lower rates of in-hospital and follow-up mortality, the rate of rehospitalization was similar, regardless of SBP. Thus, these patients are still at high risk of morbid events, and they should receive the highest quality care and education in an effort to reduce the risk of rehospitalization. The majority of patients with heart failure have elevated SBP and appear to respond favorably to in-hospital acute heart failure treatments but have typically been underrepresented in clinical trials.

These results should be evaluated in the context of several limitations. First,

OPTIMIZE-HF was not a prospective randomized trial. Unmeasured variables may have been present that could have influenced the findings. Although heart failure was determined from chart review by clinical personnel, the potential for incomplete or inaccurate classification of heart failure remains. Systolic blood pressure was not collected prior to hospital admission or after discharge; consequently, we were unable to characterize chronic changes in SBP over time. We cannot determine from these data whether SBP at admission directly influences in-hospital and short-term postdischarge outcomes or if it is simply a marker of other processes that influence outcome. In addition, as in other large heart failure cohort studies, we did not collect measures of diastolic function because reporting of these variables is not well standardized.¹³ It is possible that some patients classified as having heart failure with relatively preserved systolic function based on a heart failure symptoms, discharge diagnosis, and left ventricular ejection fraction of 40% and higher, consistent with the current heart failure guideline definition, may not have had echocardiographic evidence of diastolic dysfunction.

CONCLUSIONS

The findings from this OPTIMIZE-HF analysis indicate that SBP assessment at admission provides important, independent prognostic information in patients with heart failure with both reduced and preserved systolic function. Patients with heart failure with low SBP are at the highest risk for mortality despite the use of current pharmacological therapies. These data support previous findings from ADHERE.

Further study of the relationship between SBP in heart failure and outcomes is important and warranted; prospective studies should be designed to test the hypothesis that SBP at admission is useful for risk stratification of patients with heart failure. Elevated SBP appears to signal specific pathophysiological processes that differ from the

underlying processes in patients with low SBP. Because the characteristics and outcomes are different among patients with heart failure with varying SBP levels, management may need to vary according to SBP at admission.

Author Contributions: Drs Gheorghiadu and Fonarow had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Gheorghiadu, Abraham, Albert, Greenberg, O'Connor, Stough, Young, Fonarow.

Acquisition of data: Abraham, Albert, Greenberg, O'Connor, Young, Fonarow.

Analysis and interpretation of data: Gheorghiadu, Abraham, Greenberg, O'Connor, She, Yancy, Young, Fonarow.

Drafting of the manuscript: Gheorghiadu, Albert, Greenberg, O'Connor, She, Fonarow.

Critical revision of the manuscript for important intellectual content: Abraham, Greenberg, O'Connor, She, Yancy, Young, Fonarow.

Statistical analysis: She, Fonarow.

Obtained funding: Fonarow.

Administrative, technical, or material support: Greenberg, O'Connor, She.

Study supervision: Gheorghiadu, Abraham, Greenberg, O'Connor, Fonarow.

Financial Disclosures: Dr Gheorghiadu reported receiving research grants from the National Institutes of Health, Otsuka, Sigma Tau, Merck, and Scios Inc; being a consultant for Debbio Pharm, Errekappa Therapeutics, GlaxoSmithKline, Protein Design Labs, and Medtronic; and receiving honoraria from Abbott, AstraZeneca, GlaxoSmithKline, Medtronic, Otsuka, Protein Design Lab, Scios Inc, and Sigma Tau. Dr Abraham reported receiving research grants from Amgen, Biotronik, CHF Solutions, GlaxoSmithKline, Heart Failure Society of America, Medtronic, Myogen, the National Institutes of Health, Orqis Medical, Otsuka Maryland Research Institute, Paracor, and Scios Inc; being a consultant or serving on the speaker's bureau for

Amgen, AstraZeneca, Boehringer-Ingelheim, CHF Solutions, GlaxoSmithKline, Guidant, Medtronic, Merck, Pfizer, ResMed, Respirationics, Scios Inc, and St Jude Medical; being on the advisory board of CardioKine, CardioKinetix Inc, CHF Solutions, the Department of Veterans Affairs Cooperative Studies Program, Inovise, the National Institutes of Health, and Savacor Inc; and receiving honoraria from AstraZeneca, Boehringer-Ingelheim, GlaxoSmithKline, Guidant, Medtronic, Merck, Pfizer, ResMed, Respirationics, Scios Inc, and St Jude Medical. Dr Albert reported being a consultant for GlaxoSmithKline and Medtronic; and serving on the speaker's bureau for GlaxoSmithKline, Medtronic, NitroMed, and Scios Inc. Dr Stough reported receiving research grants from Actelion, GlaxoSmithKline, Medtronic, Otsuka, and Pfizer; being a consultant or serving on the speaker's bureau for Abbott, AstraZeneca, GlaxoSmithKline, Medtronic, Novocardia, Otsuka, Protein Design Labs, RenaMed, Sigma Tau, and Scios Inc; and receiving honoraria from Abbott, AstraZeneca, GlaxoSmithKline, Medtronic, and Pfizer. Dr Greenberg reported receiving research grant support from Abbott Laboratories, Amgen, Cardiodynamics, GlaxoSmithKline, Medicines Company, Millennium, Novocardia, Otsuka, Pfizer, Sanofi-Aventis, and Titan; serving on the speaker's bureau or being a consultant for Amgen, AstraZeneca, GlaxoSmithKline, Guidant Corp, Medtronic, Merck & Co, NitroMed, Pfizer, Remon Medical Technologies, and Scios Inc; serving on the advisory board for CHF Solutions, GlaxoSmithKline, and NitroMed; and receiving honoraria from AstraZeneca, GlaxoSmithKline, Medtronic, Merck, NitroMed, Novartis, Scios Inc, and Scios Inc. Dr O'Connor reported receiving research grant support from the National Institutes of Health; serving on the speaker's bureau and/or being a consultant for Amgen, AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Guidant, Medtronic, Merck, NitroMed, Novartis, Otsuka, Pfizer, and Scios Inc; and receiving honoraria from GlaxoSmithKline, Pfizer, and Otsuka. Dr Yancy reported receiving research grants from Cardiodynamics, GlaxoSmithKline, Scios Inc, Medtronic, and NitroMed; being a consultant or serving on the speaker's bureau for AstraZeneca, Cardiodynamics, GlaxoSmithKline, Medtronic, NitroMed, Novartis, and Scios Inc; being on the advisory board

for CHF Solutions, the Food and Drug Administration cardiovascular device panel, and the National Institutes of Health; and receiving honoraria from AstraZeneca, Cardiodynamics, GlaxoSmithKline, Medtronic, Novartis, and Scios Inc. Dr Young reported receiving research grants from Abbott, Acorn, Amgen, Artesion Therapeutics, AstraZeneca, Biosite, GlaxoSmithKline, Guidant, Medtronic, MicroMed, the National Institutes of Health, Scios Inc, Vasogen, and World Heart; and being a consultant for Abbott, Acorn, Amgen, Biomax Canada, Biosite, Boehringer-Ingelheim, Bristol-Myers Squibb, Coherix, Edwards Lifescience, GlaxoSmithKline, Guidant, Medtronic, MicroMed, Novartis, Paracor, Proctor & Gamble, Protemix, Scios Inc, Sunshine, Thoratec, Transworld Medical Corp, Vasogen, Viacor, and World Heart. Dr Fonarow reported receiving research grants from Amgen, Biosite, Bristol-Myers Squibb, Boston Scientific/Guidant, GlaxoSmithKline, Medtronic, Merck, Pfizer, Sanofi-Aventis, Scios Inc, and the National Institutes of Health; serving on the speaker's bureau or receiving honoraria from Amgen, AstraZeneca, Biosite, Bristol-Myers Squibb, Boston Scientific/Guidant, GlaxoSmithKline, Medtronic, Merck, NitroMed, Orqis Medical, Pfizer, Sanofi-Aventis, Schering-Plough, Scios Inc, and Wyeth.

Funding/Support: GlaxoSmithKline funded the OPTIMIZE-HF registry under the guidance of the OPTIMIZE-HF Steering Committee, the data collection and management by Outcome Inc, analysis of registry data at the Duke Clinical Research Institute, and administrative and material support by Accel Health. **Role of the Sponsor:** GlaxoSmithKline was involved in the design and conduct of the OPTIMIZE-HF registry and funded data collection and management through Outcome Inc, and data management and statistical analyses through the Duke Clinical Research Institute. The sponsor was not involved in the management, analysis, or interpretation of data or the preparation of the manuscript. GlaxoSmithKline reviewed the manuscript prior to submission for publication.

REFERENCES

1. Thom T, Haase N, Rosamond W, et al. Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2006;113:e85-e151.
2. Adams KF, Fonarow GC, Emerman CL, et al. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). *Am Heart J*. 2005;149:209-216.
3. Gheorghiadu M, Zannad F, Sopko G, et al. Acute heart failure syndromes: current state and framework for future research. *Circulation*. 2005;112:3958-3968.
4. Heiat A, Gross CP, Krumholz HM. Representation of the elderly, women, and minorities in heart failure clinical trials. *Arch Intern Med*. 2002;162:1682-1688.
5. VMAI Investigators. Intravenous nesiritide vs nitroglycerin for treatment of decompensated congestive heart failure: a randomized controlled trial. *JAMA*. 2002;287:1531-1540.
6. Cuffe MS, Califf RM, Adams KF Jr, et al. Short-term intravenous milrinone for acute exacerbation of chronic heart failure: a randomized controlled trial. *JAMA*. 2002;287:1541-1547.
7. Mebazaa A. The SURVIVE-W Trial: comparison of dobutamine and levosimendan on survival in acute decompensated heart failure. Presented at: American Heart Association Scientific Sessions; November 13-16, 2005; Dallas, Tex.
8. Packer M. REVIVE II: multicenter placebo-controlled trial of levosimendan on clinical status in acutely decompensated heart failure. Presented at: American Heart Association Scientific Sessions; November 13-16, 2005; Dallas, Tex.
9. Teerlink JR, McMurray JJ, Bourge RC, et al. Tezosentan in patients with acute heart failure: design of the Value of Endothelin Receptor Inhibition with Tezosentan in Acute heart failure Study (VERITAS). *Am Heart J*. 2005;150:46-53.
10. ESCAPE Investigators and ESCAPE Study Coordinators. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA*. 2005;294:1625-1633.
11. Cotter G, Kobrin I, Torre-Amione G, et al. In-hospital worsening heart failure in patients with acute heart failure: relation to renal failure, need for inotropes, CAD, hyponatremia and increased regulatory rate: a subgroup analysis from the VERITAS trial [Presented at: American Heart Association Scientific Sessions 2005; November 13-16, 2005; Dallas, Tex]. *Circulation*. 2005;112:II599.
12. Fonarow GC, Abraham WT, Albert NM, et al. Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF): rationale and design. *Am Heart J*. 2004;148:43-51.
13. Bhatia RS, Tu JV, Lee DS, et al. Outcome of heart failure with preserved ejection fraction in a population-based study. *N Engl J Med*. 2006;355:260-269.
14. Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000. *JAMA*. 2003;290:199-206.
15. Chen HH, Lainchbury JG, Senni M, Bailey KR, Redfield MM. Diastolic heart failure in the community: clinical profile, natural history, therapy, and impact of proposed diagnostic criteria. *J Card Fail*. 2002;8:279-287.
16. Levy D, Larson MG, Vasan RS, Kannel WB, Ho KK. The progression from hypertension to congestive heart failure. *JAMA*. 1996;275:1557-1562.
17. Aronson D, Mittleman MA, Burger AJ. Elevated blood urea nitrogen level as a predictor of mortality in patients admitted for decompensated heart failure. *Am J Med*. 2004;116:466-473.
18. Felker GM, Leimberger JD, Califf RM, et al. Risk stratification after hospitalization for decompensated heart failure. *J Card Fail*. 2004;10:460-466.
19. Fonarow GC, Adams KF Jr, Abraham WT, Yancy CW, Boscardin WJ. Risk stratification for in-hospital mortality in acutely decompensated heart failure: classification and regression tree analysis. *JAMA*. 2005;293:572-580.
20. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure. *JAMA*. 2003;290:2581-2587.