Published in final edited form as:

Am Heart J. 2010 July ; 160(1): 132–138.e1. doi:10.1016/j.ahj.2010.03.033.

Associations Between Worsening Renal Function and 30-Day Outcomes Among Medicare Beneficiaries Hospitalized With Heart Failure

Uptal D. Patel, MD^{a,b}, Melissa A. Greiner, MS^a, Gregg C. Fonarow, MD^c, Hemant Phatak, PhD^d, Adrian F. Hernandez, MD, MHS^{a,b}, and Lesley H. Curtis, PhD^{a,b}

^a Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC

^b Department of Medicine, Duke University School of Medicine, Durham, NC

^c Ahmanson-UCLA Cardiomyopathy Center, Department of Medicine, UCLA Medical Center, Los Angeles, CA

^d Global Outcomes Research and Reimbursement, Merck & Co., Inc., Whitehouse Station, NJ

Abstract

Background—Kidney disease is common among patients with heart failure, but relationships between worsening renal function (WRF) and outcomes after hospitalization for heart failure are poorly understood, especially among patients with preserved systolic function. We examined associations between WRF and 30-day readmission, mortality, and costs among Medicare beneficiaries hospitalized with heart failure.

Methods—We linked data from a clinical heart failure registry to Medicare inpatient claims for patients aged 65 years or older hospitalized with heart failure. We defined WRF as a change in serum creatinine ≥ 0.3 mg/dL from admission to discharge. Main outcome measures were readmission and mortality at 30 days after hospitalization and total inpatient costs.

Results—Among 20,063 patients hospitalized with heart failure, WRF was common (17.8%) and more likely among patients with higher baseline comorbidity and more impaired renal function. In unadjusted analyses, WRF was associated with similar subsequent mean inpatient costs (\$3255 vs \$3277; $p=0.2$) but higher readmission (21.8% vs 20.6%; $p=0.01$) and mortality (10.0% vs 7.2%; $p<0.001$). The differences persisted after adjustment for baseline patient and hospital characteristics (hazard of readmission, 1.10 [95% confidence interval, 1.02–1.18]; hazard of mortality, 1.53 [95% confidence interval, 1.34–1.75]). Associations of WRF with readmission and mortality were similar between patients with reduced and preserved systolic function.

Conclusions—WRF during hospitalization for heart failure is an independent predictor of early readmission and mortality in patients with reduced and preserved systolic function.

Address for correspondence: Lesley H. Curtis, PhD, Center for Clinical and Genetic Economics, Duke Clinical Research Institute, PO Box 17969, Durham, NC 27715; telephone: 919-668-8101; fax: 919-668-7124; lesley.curtis@duke.edu.

Trial Registration: clinicaltrials.gov Identifier: NCT00344513

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Introduction

The burden of acute decompensated heart failure in the United States continues to increase as the population ages and the management of coronary artery disease and the prevention of sudden cardiac death improve.^{1,2} Heart failure is the primary diagnosis in more than 1 million hospitalizations each year, and the direct and indirect costs of heart failure in 2007 were \$37.2 billion.^{1,2}

Chronic kidney disease is common among patients with heart failure and is associated with greater morbidity and mortality.³ The coexistence of heart failure and chronic kidney disease is believed to increase risk because of the comorbidity burden, toxicity from diagnostic and therapeutic procedures, and accelerated atherosclerosis. Patients with impaired kidney function are also more likely to experience acute worsening of kidney function during treatment for acute decompensated heart failure.⁴ Worsening renal function (WRF) affects 20% to 45% of patients hospitalized for heart failure.^{5–10}

Although WRF is a strong predictor of mortality,^{7,9,11} associations with costs and readmission are poorly understood, especially for patients with heart failure and preserved systolic function, because previous studies were limited by small sample sizes, retrospective study designs, suboptimal adjustment for confounders, and outdated data.^{8,12,13} We hypothesized that the incidence of WRF during hospitalization for heart failure would be similar between patients with reduced and preserved systolic function and would be associated with greater risks of postdischarge mortality, readmission, and costs to a comparable degree in these populations.

Methods

Data Sources

We accessed 2 data sources. The Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF) registry^{14,15} included clinical information for patients admitted with heart failure to 1 of 259 participating hospitals in 2003 or 2004. Patients were eligible for the registry if (a) they had symptoms of heart failure during a hospitalization for which heart failure was the primary discharge diagnosis or (b) worsening heart failure was the primary reason for the admission. Participating hospitals varied in size and geographic location. Moreover, Medicare beneficiaries in the OPTIMIZE-HF registry are similar to the broader Medicare heart failure population.^{16,17}

Research-identifiable Medicare claims data from the Centers for Medicare & Medicaid Services (CMS) included inpatient claims and corresponding denominator files for all beneficiaries discharged between 2002 and 2005. The inpatient files included institutional claims for facility costs covered under Medicare Part A; beneficiary, physician, and hospital identifiers; admission and discharge dates; and *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis and procedure codes. The denominator files included beneficiary identifier, date of birth, sex, race/ethnicity, date of death, and information about program eligibility and enrollment. We also derived index hospitalization length of stay, intensive care unit length of stay, and total Medicare payments for hospitalizations in the 365 days before the index date (expressed in 2005 US dollars).

Study Population

We included patients from OPTIMIZE-HF for whom we were able to link a registry record and an inpatient Medicare claim. Neither OPTIMIZE-HF registry data nor Medicare claims data include direct patient identifiers, so we linked the files on the basis of nonunique fields that identify unique hospitalizations when used in combination.¹⁸ We linked 29,301 (81%) of the eligible OPTIMIZE-HF hospitalizations to Medicare inpatient claims on the basis of sex,

admission date, discharge date, and hospital identifier using the earliest heart failure hospitalization. The hospitalizations represented 25,901 patients. We included only US residents aged 65 years or older who were enrolled in fee-for-service Medicare for ≥ 12 months before the hospitalization and were alive at discharge. We excluded patients with missing values for serum creatinine at admission ($n=166$ [0.6%]) or discharge ($n=3650$ [14%]) or had a history of dialysis ($n=485$ [1.9%]). The analysis data set included 20,063 patients at 232 hospitals. The institutional review board of the Duke University Health System approved the study.

Clinical Characteristics

From OPTIMIZE-HF, we obtained patient demographic characteristics, medical history, laboratory and examination measures at admission, discharge medications, and information about in-hospital procedures. For patients with missing values for systolic blood pressure (18/20,063 [0.1%]), serum sodium (54/20,063 [0.3%]), or hemoglobin (322/20,063 [1.6%]), we imputed the mean values of the overall cohort. For the missing OPTIMIZE-HF dichotomous variables left ventricular systolic dysfunction (3015/20,063 [15.0%]), smoker within the past year (634/20,063 [3.2%]), rales (307/20,063 [1.5%]), lower extremity edema (375/20,063 [1.9%]), and beta-blocker prescription at discharge (178/20,063 [0.9%]), we imputed the “no” value. We could not include other variables of interest because they were not collected (eg, blood urea nitrogen) or were missing for a large proportion of patients (eg, change in body weight between admission and discharge).

Analysis Variables

We used serum creatinine level at admission to define normal renal function (<1.5 mg/dL) and 2 categories of impaired function (1.5–1.9 mg/dL and ≥ 2.0 mg/dL). We calculated change in renal function as the difference between discharge and admission serum creatinine, and we defined WRF as a change in serum creatinine ≥ 0.3 mg/dL.^{5,10}

Outcomes

We followed patients for up to 30 days after discharge. Using the Medicare claims data, we calculated inpatient costs to Medicare by summing payment amounts and per diem adjustments from all inpatient claims (including transfers and rehabilitation claims) and adjusting to 2005 US dollars. We also calculated all-cause mortality and readmission within 30 days. We calculated time to first readmission as the number of days between the index discharge date and the subsequent readmission date, excluding transfers and admissions for rehabilitation. We obtained mortality information from the Medicare denominator files.

Statistical Analysis

We present categorical variables as frequencies and continuous variables as means with SDs or medians with interquartile ranges. To test for differences in baseline characteristics between patients with or without WRF, we used chi-square tests for categorical variables and Kruskal-Wallis tests for continuous variables. For 30-day outcomes, we compared the groups using Kruskal-Wallis tests for inpatient costs, Gray tests for readmission, and log-rank tests for mortality. To account for the competing risk of death, we used the cumulative incidence function to calculate unadjusted 30-day readmission. We used Kaplan-Meier methods to calculate unadjusted 30-day mortality.

To examine the unadjusted relationship between WRF and 30-day inpatient costs, we used a generalized linear model with a log link and a Poisson distribution. When exponentiated, cost ratios estimate the proportional increase in costs attributable to the variable. We used generalized estimating equation methods to account for the clustering of similar patients within

hospitals. We also used this approach to examine adjusted relationships and included the same baseline covariates from the multivariable models for mortality and readmission.

We used Cox proportional hazards models to examine unadjusted and adjusted relationships between WRF and 30-day readmission and mortality with robust standard errors to account for the clustering of patients within hospitals.¹⁹ In multivariable analyses, we modeled readmission and mortality as functions of WRF, age, sex, race, medical history, laboratory and examination measures at admission, medications prescribed at discharge, in-hospital procedures, inpatient costs in the prior year, intensive care unit length of stay, and a variable indicating whether the length of stay for the index hospitalization was greater than 7 days.²⁰

We performed 2 secondary analyses. First, we repeated the analysis by type of heart failure (ie, preserved vs reduced systolic function), because previous studies have reported conflicting results.^{7,21} Second, we categorized WRF in 0.1 mg/dL increments of serum creatinine and examined associations between categories of WRF and 30-day outcomes.

We used SAS version 9.2 for all analyses (SAS Institute Inc, Cary, NC).

Results

The analysis included 20,063 patients from 232 hospitals; 3581 (17.8%) had WRF during the index hospitalization (Table 1). Baseline characteristics were similar between patients with or without WRF. However, patients with WRF were more likely to be black and to have diabetes mellitus, hyperlipidemia, peripheral vascular disease, and prior cerebrovascular disease. They were less likely to have left ventricular systolic dysfunction (33.3% vs. 36.7%; $p<0.001$). Patients with WRF were more likely to have higher serum creatinine levels and longer length of stay. Baseline characteristics also were similar between patients with or without preserved systolic function (**Appendix**). The frequency of WRF was slightly higher in patients with preserved systolic function (18.6% vs 16.5%; $p<0.001$).

Despite longer lengths of stay among patients with WRF, mean inpatient costs 30 days after the index hospitalization were similar between patients with WRF and those without (Table 2). These estimates corresponded to an unadjusted cost ratio of 1.00 (95% confidence interval [CI], 0.90–1.11) and were similar after adjustment for potential confounders (1.02; 95% CI, 0.92–1.13).

WRF was a predictor of higher cumulative incidence of all-cause readmission and mortality at 30 days. Readmission rates were 21.8% among patients with WRF and 20.6% among those without. The hazard ratio (HR) for readmission was approximately 10% greater among patients with WRF (1.09; 95% CI, 1.01–1.18), even after adjustment for potential confounders. Similarly, 30-day all cause mortality was higher among patients with WRF (10.0% vs. 7.2%; $p<0.001$), conferring an increased risk of approximately 40% (HR, 1.41; 95% CI, 1.23–1.60). This difference persisted after adjustment for patient- and hospital-level characteristics (HR, 1.53; 95% CI, 1.34–1.75).

To determine whether associations between WRF and outcomes were influenced by the type of heart failure, we examined outcomes among patients with preserved systolic function ($n=12,817$ [63.9%]) and patients with left ventricular systolic dysfunction ($n=7246$ [36.1%]). The direction and magnitude of the associations were similar between the groups (Table 3). However, WRF was associated with a 15% increase in inpatient costs among patients with systolic dysfunction.

To determine whether there was a threshold effect for the severity of WRF, we examined associations between incremental values of WRF and 30-day outcomes (Table 4). Readmission

and mortality were highest among patients with a change in serum creatinine ≥ 0.5 mg/dL. However, the rates were among the lowest in the group with a 0.4–0.5 mg/dL change in serum creatinine, and they were among the highest among patients with a change in serum creatinine < 0.1 mg/dL. These patterns disrupted what would otherwise have been a monotonic trend of increasing risks of readmission and mortality associated with increasing changes in serum creatinine level. Similarly, a trend of increasing inpatient costs across categories of WRF was disrupted by patients with changes in serum creatinine < 0.1 mg/dL and 0.2–0.3 mg/dL.

Finally, when we included baseline renal function in the multivariable models, WRF remained an important predictor of outcomes. In the case of readmission, WRF (HR, 1.10; 95% CI, 1.02–1.18) was a weaker predictor than admission serum creatinine ≥ 2.0 mg/dL (HR, 1.34; 95% CI, 1.21–1.47). In the case of mortality, WRF (HR, 1.53; 95% CI, 1.34–1.75) was nearly as strong a predictor as serum creatinine ≥ 2.0 mg/dL (HR, 1.58; 95% CI, 1.38–1.81).

Discussion

In a large, contemporary cohort of patients hospitalized with heart failure, the prevalence of WRF was high, particularly among patients with greater comorbidity and impaired baseline kidney function. Patients with preserved systolic function had a slightly higher incidence of WRF than patients with systolic dysfunction. WRF was associated with similar mean inpatient costs but higher readmission and mortality rates at 30 days. These associations were comparable in patients with reduced and preserved systolic function. However, WRF was associated with a trend toward higher inpatient costs among patients with systolic dysfunction, but not among those with preserved systolic function. These findings highlight the importance of including kidney function in studies of readmission and mortality among patients with heart failure. Patient-level measures of kidney function may not be adequately considered in hospital-specific 30-day mortality rates reported through quality-improvement efforts for heart failure.

Changes in serum creatinine level as small as 0.1–0.2 mg/dL are common and are associated with an increased risk of death,^{7–11} as is greater severity of WRF.⁹ When we examined associations between WRF and readmission and mortality, the findings were consistent with this pattern. Moreover, the magnitude of the associations was similar to previous findings and was independent of baseline renal function. For example, the hazard of mortality of 1.53 is similar to findings from a meta-analysis of 18,634 patients with WRF (pooled odds ratio, 1.48; 95% CI, 1.35–1.63).⁹ However, the 3 studies in the meta-analysis that included 30-day outcomes^{7,12,13} had various definitions of WRF, sample sizes, study designs, and patient characteristics.²² The pooled odds ratio was 1.88 (95% CI, 1.26–2.81).

We defined WRF as the difference between admission and discharge serum creatinine. Most studies have used a change of ≥ 0.3 mg/dL or > 0.3 mg/dL^{7,9,11}; however, change in serum creatinine can be calculated as the difference between the admission value and either the peak level or the discharge level. Use of the peak level allows greater sensitivity, because the discharge value is likely to normalize from the peak value in many patients hospitalized for heart failure. Nonetheless, both definitions have been used in the literature without clarification from studies that assess differences in associations with adverse outcomes. Our use of the less sensitive value based on discharge level may account for the slightly lower prevalence of WRF we observed (18% vs 20%–45%).^{5–9} On the other hand, our definition may have included patients with greater renal impairment, thus accounting for other associations we observed. In contrast to studies that did not find an association between WRF and readmission,^{8,12,13} we found that 30-day readmission was approximately 10% higher. In addition, shorter length of stay in our study may reflect earlier discharges leading to a greater likelihood of readmission.^{7,10,13}

Despite finding greater risks of short-term readmission and mortality, we did not observe significant differences in inpatient costs between patients with or without WRF. Costs of the index hospitalization were not included in the 30-day cost estimates because we were interested in examining the association between WRF and subsequent inpatient costs. Previous studies that have reported inpatient costs evaluated costs for the index hospitalization rather than costs after discharge.⁷ Because of longer lengths of stay among patients with WRF, differences in index hospitalization costs can be expected.

Many previously reported associations between WRF and patient characteristics were also observed in this study, including severity of baseline kidney disease, comorbid conditions, and physical examination findings, including elevated systolic blood pressure and basilar rales.^{7, 11} Most of these characteristics are not modifiable, but they may contribute to underlying pathophysiological mechanisms thought to exacerbate WRF, particularly in patients receiving diuretics.^{7,9,11,23,24} However, we also found a lower prevalence of WRF among patients with systolic dysfunction, consistent with one previous study.⁷ Other studies have been mixed, some reporting a higher prevalence among patients with systolic dysfunction²¹ and others finding no association.¹¹ In addition, we found similar associations between WRF and 30-day outcomes among patients with systolic dysfunction and those without. These findings support recent developments in the understanding of heart failure pathophysiology that are less likely to implicate impaired cardiac output and inadequate arterial filling and more likely to implicate venous congestion and elevated intra-abdominal pressure.^{4,24–26} Consequently, several renal-sparing treatment strategies are being evaluated in clinical trials.^{4,26}

Associations between WRF and 30-day readmission and mortality have several implications. First, as a strong independent predictor of readmission and death, WRF may offer a target for interventions to reduce readmission and mortality rates associated with acute decompensated heart failure. Second, quality-improvement and public reporting initiatives do not adequately consider kidney function in assessments of mortality. For example, CMS has reported 30-day hospital-specific mortality for patients with heart failure in the Hospital Compare program.²⁷ Although these rates are risk-standardized, the measures rely on claims data that lack detailed information about baseline kidney function or changes during hospitalization. Moreover, patients with more severe renal dysfunction are less likely to receive guideline-recommended therapies.²⁸ Failure to account for such treatment bias may limit the validity of hospital-specific outcomes. In our study, patients with WRF were less likely to receive angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers at discharge. Consideration of variations in patient-level case mix will require data on changes in kidney function during heart failure hospitalizations.

Our study has some limitations. First, clinical data were collected from medical records and depended upon the accuracy and completeness of clinical documentation. Exposure misclassification for WRF may have occurred if differences in serum creatinine levels during index hospitalizations were not reflected in discharge levels. This bias may have led to underestimates of associations with study outcomes.²⁹ Moreover, changes in renal function in patients with heart failure are multifactorial, potentially related to inadequate arterial filling, medication toxicity, tubular injury, venous congestion, or a combination of mechanisms, none of which we could specify. Although serum creatinine measurements were not standardized across hospitals, any resulting exposure misclassification should be distributed randomly. Second, misclassification for 30-day outcomes may have resulted from inaccurate links to Medicare data; however, the linking method has been well-validated,^{16,18} and links to Medicare data permitted assessment of important 30-day outcomes. Third, the findings may not apply to hospitals that differed in patient characteristics or care patterns from OPTIMIZE-HF hospitals. We employed robust analytic methods to account for site clustering effects in a this large, contemporary cohort study, the largest single prospective evaluation of outcomes

associated with WRF. Fourth, claims-based cost data may not reflect actual costs. Finally, although we identified associations between WRF and 30-day outcomes, we could not identify the mechanisms for these associations.

In conclusion, WRF is an important independent predictor of short-term readmission and mortality among patients hospitalized with heart failure. These associations are similar between patients with systolic dysfunction and those without. Our findings highlight the importance of assessing changes in renal function during hospitalization to identify patients at high risk for early readmission and mortality.

Acknowledgments

Funding/Support

This study was funded by an unrestricted educational grant from Merck & Co. The OPTIMIZE-HF registry was funded by GlaxoSmithKline. Dr Patel was supported by grant K23DK075929 from the National Institute of Diabetes and Digestive and Kidney Diseases; Dr Hernandez by American Heart Association Pharmaceutical Roundtable grant 0675060N; and Dr Fonarow by the Ahmanson Foundation and the Corday Family Foundation. The contents of this manuscript are solely the responsibility of the authors and do not necessarily represent the official views of the National Institute of Diabetes and Digestive and Kidney Diseases or the National Institutes of Health.

We thank Damon M. Seils, MA, Duke University, for assistance with manuscript preparation. Mr Seils did not receive compensation for his assistance apart from his employment at the institution where the study was conducted.

References

1. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart Disease and Stroke Statistics--2009 Update: A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2009;119:e21–181. [PubMed: 19075105]
2. Fang J, Mensah GA, Croft JB, Keenan NL. Heart failure-related hospitalization in the U.S. 1979 to 2004. *J Am Coll Cardiol* 2008;52:428–34. [PubMed: 18672162]
3. Ezekowitz J, McAlister FA, Humphries KH, et al. The association among renal insufficiency, pharmacotherapy, and outcomes in 6,427 patients with heart failure and coronary artery disease. *J Am Coll Cardiol* 2004;44:1587–92. [PubMed: 15489090]
4. Gheorghiade M, Pang PS. Acute heart failure syndromes. *J Am Coll Cardiol* 2009;53:557–73. [PubMed: 19215829]
5. Nohria A, Hasselblad V, Stebbins A, et al. Cardiorenal interactions: insights from the ESCAPE trial. *J Am Coll Cardiol* 2008;51:1268–74. [PubMed: 18371557]
6. Klein L, Massie BM, Leimberger JD, et al. Admission or changes in renal function during hospitalization for worsening heart failure predict postdischarge survival: results from the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF). *Circ Heart Fail* 2008;1:25–33. [PubMed: 19808267]
7. Krumholz HM, Chen YT, Vaccarino V, et al. Correlates and impact on outcomes of worsening renal function in patients > or =65 years of age with heart failure. *Am J Cardiol* 2000;85:1110–3. [PubMed: 10781761]
8. Smith GL, Vaccarino V, Kosiborod M, et al. Worsening renal function: what is a clinically meaningful change in creatinine during hospitalization with heart failure? *J Card Fail* 2003;9:13–25. [PubMed: 12612868]
9. Damman K, Navis G, Voors AA, et al. Worsening renal function and prognosis in heart failure: systematic review and meta-analysis. *J Card Fail* 2007;13:599–608. [PubMed: 17923350]
10. Gottlieb SS, Abraham W, Butler J, et al. The prognostic importance of different definitions of worsening renal function in congestive heart failure. *J Card Fail* 2002;8:136–41. [PubMed: 12140805]
11. Forman DE, Butler J, Wang Y, et al. Incidence, predictors at admission, and impact of worsening renal function among patients hospitalized with heart failure. *J Am Coll Cardiol* 2004;43:61–7. [PubMed: 14715185]

12. Cowie MR, Komajda M, Murray-Thomas T, Underwood J, Ticho B. Prevalence and impact of worsening renal function in patients hospitalized with decompensated heart failure: results of the prospective outcomes study in heart failure (POSH). *Eur Heart J* 2006;27:1216–22. [PubMed: 16624834]
13. Akhter MW, Aronson D, Bitar F, et al. Effect of elevated admission serum creatinine and its worsening on outcome in hospitalized patients with decompensated heart failure. *Am J Cardiol* 2004;94:957–60. [PubMed: 15464689]
14. 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. [PubMed: 15215791]
15. Fonarow GC, Abraham WT, Albert NM, et al. Association between performance measures and clinical outcomes for patients hospitalized with heart failure. *JAMA* 2007;297:61–70. [PubMed: 17200476]
16. Curtis LH, Greiner MA, Hammill BG, et al. Representativeness of a national heart failure quality-of-care registry: comparison of OPTIMIZE-HF and non-OPTIMIZE-HF Medicare patients. *Circ Cardiovasc Qual Outcomes* 2009;2:377–84. [PubMed: 20031864]
17. Arday SL, Arday DR, Monroe S, Zhang J. HCFA's racial and ethnic data: current accuracy and recent improvements. *Health Care Financ Rev* 2000;21:107–16. [PubMed: 11481739]
18. Hammill BG, Hernandez AF, Peterson ED, Fonarow GC, Schulman KA, Curtis LH. Linking inpatient clinical registry data to Medicare claims data using indirect identifiers. *Am Heart J* 2009;157:995–1000. [PubMed: 19464409]
19. Lin DY, Wei LJ. The robust inference for the Cox proportional hazards model. *J Am Stat Assoc* 1989;84:1074–8.
20. Krumholz HM, Parent EM, Tu N, et al. Readmission after hospitalization for congestive heart failure among Medicare beneficiaries. *Arch Intern Med* 1997;157:99–104. [PubMed: 8996046]
21. de Silva R, Nikitin NP, Witte KK, et al. Incidence of renal dysfunction over 6 months in patients with chronic heart failure due to left ventricular systolic dysfunction: contributing factors and relationship to prognosis. *Eur Heart J* 2006;27:569–81. [PubMed: 16364971]
22. Damman K, Navis G, Smilde TD, et al. Decreased cardiac output, venous congestion and the association with renal impairment in patients with cardiac dysfunction. *Eur J Heart Fail* 2007;9:872–8. [PubMed: 17586090]
23. Hasselblad V, Gattis Stough W, Shah MR, et al. Relation between dose of loop diuretics and outcomes in a heart failure population: results of the ESCAPE trial. *Eur J Heart Fail* 2007;9:1064–9. [PubMed: 17719273]
24. Mullens W, Abrahams Z, Skouri HN, et al. Elevated intra-abdominal pressure in acute decompensated heart failure: a potential contributor to worsening renal function? *J Am Coll Cardiol* 2008;51:300–6. [PubMed: 18206740]
25. Jessup M, Costanzo MR. The cardiorenal syndrome: Do we need a change of strategy or a change of tactics? *J Am Coll Cardiol* 2009;53:597–9. [PubMed: 19215834]
26. Tang, WH.; Mullens, W. Cardio-renal syndrome in decompensated heart failure. *Heart*. (Epub ahead of print: <http://dx.doi.org/10.1136/hrt.2009.166256>)
27. US Department of Health and Human Services. Hospital Compare. [Accessed May 4, 2009]. Available at: <http://www.hospitalcompare.hhs.gov>
28. Patel UD, Hernandez AF, Liang L, et al. Quality of care and outcomes among patients with heart failure and chronic kidney disease: A Get With the Guidelines–Heart Failure Program study. *Am Heart J* 2008;156:674–81. [PubMed: 18946892]
29. Flegal KM, Brownie C, Haas JD. The effects of exposure misclassification on estimates of relative risk. *Am J Epidemiol* 1986;123:736–51. [PubMed: 3953551]

Table 1**Baseline Characteristics of the Study Population by Renal Function**

Characteristic	Change in Serum Creatinine Level ^a		p Value
	<0.3 mg/dL (n=16,482)	≥0.3 mg/dL (n=3581)	
Age, mean (SD), y	79.6 (7.8)	79.8 (7.7)	0.42
Male sex, No. (%)	7249 (44.0)	1544 (43.1)	0.34
Race, No. (%)			
Black	1660 (10.1)	405 (11.3)	0.03
Nonblack	14,822 (89.9)	3,176 (88.7)	0.03
Medical history, No. (%)			
Anemia	3038 (18.4)	738 (20.6)	0.003
Atrial arrhythmia	6194 (37.6)	1169 (32.6)	<0.001
Chronic obstructive pulmonary disease	4717 (28.6)	1060 (29.6)	0.24
Chronic renal insufficiency	2849 (17.3)	967 (27.0)	<0.001
Depression	1779 (10.8)	378 (10.6)	0.68
Diabetes mellitus	6340 (38.5)	1471 (41.1)	0.004
Heart failure with ischemic etiology	7921 (48.1)	1750 (48.9)	0.38
Hyperlipidemia	5372 (32.6)	1258 (35.1)	0.003
Hypertension	11,641 (70.6)	2719 (75.9)	<0.001
Left ventricular systolic dysfunction	6052 (36.7)	1194 (33.3)	<0.001
Peripheral vascular disease	2398 (14.5)	596 (16.6)	0.001
Prior cerebrovascular accident or transient ischemic attack	2831 (17.2)	685 (19.1)	0.005
Pulmonary reactive airway disease	777 (4.7)	184 (5.1)	0.28
Smoker in previous year	1529 (9.3)	318 (8.9)	0.46
Thyroid abnormality	2859 (17.3)	680 (19.0)	0.02
Admission characteristics			
Beta-blocker at admission, No (%)	8763 (53.2)	1913 (53.4)	0.78
Hemoglobin level, mean (SD), g/dL	12.0 (2.0)	11.8 (1.9)	<0.001
Lower extremity edema, No. (%)	10,481 (63.6)	2317 (64.7)	0.21
Rales, No. (%)	10,548 (64.0)	2391 (66.8)	0.002
Serum creatinine level, mean (SD), mg/dL, No. (%)	1.5 (0.9)	1.6 (1.0)	<0.001
<1.5 mg/dL	9786 (59.4)	1995 (55.7)	<0.001
1.5–1.9 mg/dL	3474 (21.1)	799 (22.3)	0.10
≥2.0 mg/dL	3222 (19.5)	787 (22.0)	0.001
Serum sodium level, mean (SD), mEq/L	137.7 (4.9)	138.0 (4.8)	<0.001
Systolic blood pressure, mean (SD), mm Hg	140.9 (30.8)	149.5 (32.5)	<0.001
Discharge medications, No. (%)			
Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker	10,189 (61.8)	2076 (58.0)	<0.001
Aldosterone antagonist	1900 (11.5)	392 (10.9)	0.32
Antiplatelet agent	8659 (52.5)	1955 (54.6)	0.03
Beta-blocker	10,360 (62.9)	2272 (63.4)	0.51
Digoxin	4939 (30.0)	816 (22.8)	<0.001

Characteristic	Change in Serum Creatinine Level ^a		p Value
	<0.3 mg/dL (n=16,482)	≥0.3 mg/dL (n=3581)	
Diuretic	13,712 (83.2)	2899 (81.0)	0.001
Lipid-lowering agent	5847 (35.5)	1408 (39.3)	<0.001
Characteristics of index hospitalization			
Length of stay, mean (SD), d	5.6 (4.7)	6.3 (4.8)	<0.001
Intensive care unit length of stay, mean (SD), d	1.2 (3.0)	1.3 (3.4)	0.22
Inpatient costs to Medicare in previous year, mean (SD), \$	12,924 (20,656)	12,267 (19,846)	0.11
None, No. (%)	6239 (37.9)	1391 (38.8)	0.27
≤ \$8000, No. (%)	3417 (20.7)	736 (20.6)	0.81
\$8001–\$21,000, No. (%)	3387 (20.5)	764 (21.3)	0.29
>\$21,000, No. (%)	3439 (20.9)	690 (19.3)	0.03

^aPatients with a change in serum creatinine ≥ 0.3 mg/dL during the index hospitalization were considered to have worsening renal function.

Table 2

Outcomes at 30 Days by Change in Serum Creatinine Level

Outcome	Change in Serum Creatinine Level ^a		P Value	Unadjusted (95% CI)	Adjusted (95% CI)	p Value
	<0.3 mg/dL (n=16,482)	≥0.3 mg/dL (n=3581)				
Inpatient costs, mean (SD), \$ ^b	3277 (10,178)	3255 (8893)	0.2	1.00 (0.90–1.11)	1.02 (0.92–1.13)	0.7
Readmission, No. (%) ^c	3402 (20.6)	784 (21.8)	0.01	1.09 (1.01–1.18)	1.10 (1.02–1.18)	0.02
Mortality, No. (%) ^d	1190 (7.2)	357 (10.0)	<0.001	1.41 (1.23–1.60)	1.53 (1.34–1.75)	<0.001

CI = confidence interval.

^aPatients with a change in serum creatinine ≥ 0.3 mg/dL during the index hospitalization were considered to have worsening renal function.

^bCosts adjusted to 2005 US dollars, excluding index hospitalization costs. Unadjusted and adjusted values represented by cost ratios.

^cCumulative incidence of all-cause readmission. Unadjusted and adjusted values represented by hazard ratios.

^dAll-cause mortality. Unadjusted and adjusted values represented by hazard ratios.

Table 3
Associations Between Worsening Renal Function and 30-Day Outcomes by Type of Heart Failure

Outcome	Preserved Systolic Function (n=12,817)		Left Ventricular Systolic Dysfunction (n=7246)	
	Unadjusted	Adjusted	Unadjusted	Adjusted
Inpatient costs ^a	0.94 (0.81–1.09)	0.95 (0.82–1.09)	1.11 (0.95–1.30)	1.15 (0.99–1.33)
Readmission ^b	1.09 (1.00–1.19)	1.08 (0.98–1.18)	1.10 (0.96–1.27)	1.12 (0.97–1.29)
Mortality ^b	1.39 (1.16–1.66)	1.54 (1.28–1.85)	1.46 (1.18–1.80)	1.50 (1.21–1.86)

^aUnadjusted and adjusted values represented by cost ratios with 95% confidence intervals, based on costs excluding index hospitalization costs.

^bUnadjusted and adjusted values represented by hazards ratios with 95% confidence intervals.

Table 4

Outcomes at 30 Days by Incremental Categories of Worsening Renal Function

Outcome	Change in Serum Creatinine Level, mg/dL						
	<0.1	0.1 to <0.2	0.2 to <0.3	0.3 to <0.4	0.4 to <0.5	≥0.5	p Value
n	12,526	2871	1085	1449	401	1731	
Inpatient costs, \$ ^a	3389 (9880)	2784 (8907)	3286 (15,373)	2906 (7626)	3178 (11,613)	3565 (9143)	<0.001
Readmission, No. (%) ^b	2661 (21.2)	534 (18.6)	207 (19.0)	305 (21.0)	71 (17.6)	408 (23.5)	0.006
Mortality, No. (%) ^c	965 (7.7)	150 (5.2)	75 (6.9)	103 (7.1)	24 (6.0)	230 (13.3)	<0.001

^aCosts adjusted to 2005 US dollars, excluding index hospitalization costs. Unadjusted and adjusted values represented by cost ratios.^bCumulative incidence of all-cause readmission. Unadjusted and adjusted values represented by hazard ratios.^cAll-cause mortality. Unadjusted and adjusted values represented by hazard ratios.