

Trends in In-Hospital Mortality, Length of Stay, Nonroutine Discharge, and Cost Among End-Stage Renal Disease Patients on Dialysis Hospitalized With Heart Failure (2001–2014)

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ABSTRACT

Background: Heart failure (HF) is a common cause of morbidity and mortality among end-stage renal disease (ESRD) patients on dialysis. We aimed to assess the trends and outcomes in primary and secondary HF hospitalizations among ESRD patients with the use of a nationally representative database.

Methods and Results: We analyzed data from the National Inpatient Sample and the US Census Bureau to calculate annual national rates of in-hospital mortality, length of stay, disposition with a focus on non-routine discharge (discharge to a health care facility rather than to home), and adjusted median cost among patients with ESRD on dialysis with primary or secondary HF admissions from 2001 to 2014. An estimated 812,090 primary and 2,887,432 secondary HF admissions occurred from 2001 to 2014. The prevalence of comorbidities increased during the study period. Primary HF admission rates increased from 2001 to 2006 and decreased from 2007 to 2014, whereas secondary HF admissions increased significantly during the study period ($P < .001$). We found statistically significant declines of primary and secondary admission in-hospital mortality, with annual percentage changes of -3.1% and -2.6% respectively ($P < .001$ for both). In addition, the lengths of stay decreased significantly for primary and secondary HF admissions ($P < .001$ for both). However, nonroutine discharges increased significantly for both. Subgroup analysis showed higher in-hospital mortality for men, patients >65 years of age, whites, and those on peritoneal dialysis. The cost of hospitalization did not change significantly for primary and secondary HF admissions.

Conclusion: Among ESRD patients on dialysis with primary or secondary HF admission diagnosis, comorbidity prevalence increased but in-hospital mortality and length of stay decreased significantly from 2001 to 2014. (*J Cardiac Fail* 2019;25:524–533)

Key Words: Heart failure, end-stage renal disease, in-hospital mortality.

Heart failure (HF) and end-stage renal disease (ESRD) are leading causes of morbidity and mortality. Patients with HF suffer from multiple comorbidities that further increase their morbidity and mortality.^{1–3} A large proportion of HF patients have varying degrees of renal dysfunction, from mild chronic kidney disease to ESRD requiring dialysis. Patients with ESRD are at increased risk for cardiovascular (CV) events; CV mortality and morbidity are ~ 2 – 10 times higher than in individuals with normal renal function.^{4,5}

Among patients on hemodialysis (HD), heart disease is the leading cause of mortality.⁶ It is estimated that patients on dialysis have 8% higher mortality than the general population and that CV mortality accounts for approximately one-half of those deaths.⁷ Although CV mortality rates have decreased in the general population, this does not apply to ESRD patients.⁴

Approximately one-third of patients with ESRD have HF at initiation of dialysis, and 25% of patients with ESRD develop HF while on dialysis.^{8–11} The 3-year survival rate of patients on dialysis after diagnosis of HF is $<20\%$.⁸ Among patients with ESRD, poor volume control, uncontrolled hypertension, progression of coronary artery disease, anemia, electrolytic abnormalities, myocardial fibrosis,¹² and uremic toxins^{13,14} lead to development of HF and hospitalization with HF exacerbation. Therapeutic strategies that effectively reduce HF hospitalizations and mortality in the general HF population offer limited benefit in this group. Despite advances in treatment of ESRD patients with HF,^{15,16} clinical outcomes have not changed substantially.

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Most studies have evaluated the outcomes of worsening renal function or development of acute kidney injury (AKI) requiring hemodialysis during the HF hospitalization, and data on in-hospital outcomes of ESRD patients hospitalized with HF are limited. We sought to evaluate in-hospital trends and outcomes of HF hospitalizations among ESRD patients. For this purpose, we selected a large nationally representative database of hospital admissions and analyzed pertinent in-hospital outcomes, such as mortality, length of stay, nonroutine discharge (discharge to a health care facility rather than to home), and hospitalization cost, in the overall population of ESRD patients with HF as well as in subgroups of patients over 65 years of age, those on peritoneal dialysis, women, and nonwhite patients.

Methods

Data Source and Study Population

Data from the National Inpatient Sample (NIS) of the Healthcare Cost and Utilization project (HCUP), Agency of Health Care Research and Quality (AHRQ), and the US Census Bureau were used to conduct this study. The design and description of the NIS have been previously reported online.¹⁷ Briefly, the NIS is the largest all-payer inpatient care database in the United States. This nationally representative database includes yearly encounter information of hospital stays and data on patient- and hospital-level characteristics for each hospitalization. In addition, patient-level factors including demographics, diagnosis, comorbidities, and disposition with a focus on nonroutine discharge and hospital-level factors including bed size, location, and total number of hospitalizations are available in this dataset.

Patient Population

All adult patients (aged ≥ 18 years) with ESRD requiring dialysis (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] diagnosis codes 585.6, 39.95, and 54.98) admitted with a primary or secondary diagnosis of HF in the years 2001–2014 were included in the analysis. A primary HF diagnosis refers to hospitalizations mainly attributable to HF and was identified via the ICD-9-CM codes 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, and 428.12, as recommended by the American College of Cardiology (ACC)/American Heart Association (AHA) task force on performance measures.¹⁸ A secondary HF diagnosis refers to hospitalizations of patients with chronic HF who were admitted for reasons other than HF. HF was classified as a primary diagnosis if any of the codes appear as the first diagnosis in the NIS database and secondary if the codes appear at any other level of diagnosis. We excluded patients with earlier stages of chronic kidney disease and those requiring dialysis in the setting of AKI (ICD-9-CM codes 584.5 and 584.9).

End Points

The main end points in the study included annual national rates of in-hospital mortality, length of stay, non-routine discharge, and cost of hospitalization.

Statistical Analysis

National estimates including incidence, mean, and rates were calculated using the hospital trend weight provided by AHRQ. To quantify comorbidities per hospitalization, we used the Elixhauser comorbidity index to identify and classify coexisting conditions.^{19,20} Baseline characteristics across years grouped into 5 consecutive categories were compared by means of chi-square test for categorical variables and analysis of variance or Kruskal-Wallis test (as appropriate) for continuous variables. Hospitalization cost was inflation-adjusted to the currency value of 2014 with the use of the consumer price indices provided by the US Bureau of Labor statistics. To assess for trends across the years, we used a Poisson regression model to evaluate change in number of admissions per year, a mixed-effect logistic model for hospitalization outcomes, and a linear mixed model for length of stay and cost. For each model, linear temporal trend was evaluated by including year of data collection as a continuous independent variable in the same model as the outcome of interest, and the significance of the trend was based on the Wald test. Finally, subgroup analysis by type of dialysis was conducted with the use of a hierarchic mixed-effect model. Given that patient-level factors are nested within hospital-level factors, we built a hierarchic model with unique hospital identification number as random effect in the model. Potential confounding variables, including age, sex, race, dialysis type, comorbidities including hypertension, diabetes, ischemic cardiomyopathy, chronic lung disease, anemia, obesity, and chronic liver disease, hospital characteristics including teaching status and bed size, socioeconomic status, and primary payer were adjusted for. All analyses were performed with the use of Stata 14 (Statacorp, College Station, Texas), with 2-tailed level of significance set at 0.05.

Results

An estimated 812,090 primary and 2,887,432 secondary HF admissions occurred during the study period. The demographic, patient, and hospital characteristics of this cohort are presented in [Table 1](#) for primary HF admissions and in [Supplemental Table 1](#) for secondary HF admissions. The number of primary HF admissions increased and peaked during the years 2006–2009 and then decreased, with a nonsignificant average annual percentage change of +0.53% ($P = .49$; [Fig. 1](#)). Secondary HF admissions increased significantly during the study period, with an average annual percentage change of +7.8% ($P < .001$; [Fig. 2](#)). The mean age of patients was 65 years, and women accounted for ~49% of the population. Overall, the percentage of white ESRD

Table 1. Baseline Characteristics of Primary Heart Failure Admissions, %

Characteristic	Total	2001–2003	2004–2006	2007–2009	2010–2012	2013–2014	<i>P</i> Value
No. of patients (unweighted)	170,331	32,332	39,140	40,253	37,556	21,050	
No. of patients (weighted)	812,089	151,527	184,055	191,377	179,880	105,250	
Age, y, mean (SD)	65.0 (14.4)	64.4 (14.4)	64.3 (14.6)	65.1 (14.6)	65.5 (14.2)	65.4 (14.1)	<.001
Age categories							
<65 y	44.85	44.48	46.30	44.81	44.03	44.27	
≥65 y	55.15	55.52	53.70	55.19	55.97	55.73	
Female, %	49.0	50.91	49.68	49.06	47.58	47.36	<.001
Race/ethnicity							<.001
White	45.20	44.73	45.02	46.18	44.54	45.58	
Black	35.12	34.60	34.06	34.57	36.82	35.30	
Hispanic	15.71	16.65	17.24	15.26	14.78	14.60	
Asian	3.97	4.01	3.68	3.99	3.85	4.52	
Dialysis type							<.001
Hemodialysis	97.79	97.36	97.64	98.36	97.98	97.41	
Peritoneal dialysis	2.21	2.64	2.36	1.64	2.02	2.59	
Peripheral vascular disease	15.43	13.51	13.75	15.40	17.00	17.80	<.001
Hypertension	72.29	39.06	74.53	77.00	79.51	80.15	
Diabetes	55.15	52.57	51.75	54.75	57.74	60.28	<.001
Obese	8.08	3.69	4.68	7.49	11.31	14.20	<.001
Anemia	48.81	36.65	36.48	47.17	59.34	68.52	<.001
Chronic pulmonary disease	30.00	25.28	27.81	29.70	32.37	35.21	<.001
Renal failure							
Liver disease	3.50	2.51	2.90	3.27	4.11	5.00	<.001
Coagulopathy	5.40	2.83	3.62	5.16	7.31	8.38	<.001
Malignancy	0.55	0.53	0.54	0.52	0.58	0.58	.71
Elixhauser score							<.001
0–1	3.09	9.10	3.97	1.93	1.37	0.59	
2–3	32.97	49.74	40.20	32.90	24.42	17.78	
≥4	63.95	41.16	55.84	65.17	74.21	81.63	
Ischemic cardiomyopathy	50.78	46.18	47.52	50.68	54.93	56.69	
Median household income by zip code							<.001
1st quartile	37.48	34.86	37.73	37.59	38.68	38.73	
2nd quartile	25.42	26.85	25.33	25.50	24.14	25.50	
3rd quartile	21.01	22.35	20.34	20.14	21.70	20.62	
4th quartile	16.09	15.94	16.60	16.77	15.47	15.15	
Expected primary payer							<.001
Medicare	79.28	78.02	79.04	79.10	80.45	79.96	
Medicaid	9.62	9.69	10.21	9.39	9.12	9.75	
Private	9.04	10.34	8.74	9.36	8.43	8.11	
Self-pay	0.99	0.85	1.06	1.05	0.99	0.98	
Hospital size (by no. of beds)							<.001
Small	9.62	7.95	8.97	9.20	9.99	13.51	
Medium	24.76	24.11	23.82	24.14	24.70	28.85	
Large	65.62	67.94	67.22	66.66	65.31	57.64	
Hospital location							<.001
Rural	7.97	8.61	6.28	8.95	8.62	7.08	
Urban nonteaching	47.74	50.08	53.15	48.24	45.81	36.57	
Urban teaching	44.30	41.31	40.57	42.81	45.57	56.35	

patients was lower than the percentage of this subgroup in the general population of patients admitted with HF, as reported in our previous analysis,²¹ whereas the percentage of black patients with ESRD was higher. Most patients (~97%) were on hemodialysis, and the remaining were on peritoneal dialysis. The prevalence of comorbid conditions including hypertension, diabetes, obesity, chronic pulmonary disease, anemia, liver, and peripheral vascular disease (from which we estimated the Elixhauser score for each case), increased significantly during the study period (Table 1; Supplemental Table 1), suggesting that ESRD patients admitted with HF are becoming sicker with time. During the study period, the number of admissions in small, medium-size

hospitals, and urban teaching centers increased significantly.

Outcomes

In-hospital mortality among patients hospitalized with a primary diagnosis of HF declined from 4.38% in 2001 to 3.15% in 2014, with an average annual percentage change of -3.1% ($P < .001$; Fig. 3). In-hospital mortality rates plateaued over the last 3 years of the analysis, with the lowest rate reported in 2011 (2.71%). Trends of in-hospital mortality categorized in 5 different eras (2001–03, 2004–06, 2007–09, 2010–2012, and 2013–14) are presented in Supplemental Table 2. In stratified analysis, in-hospital

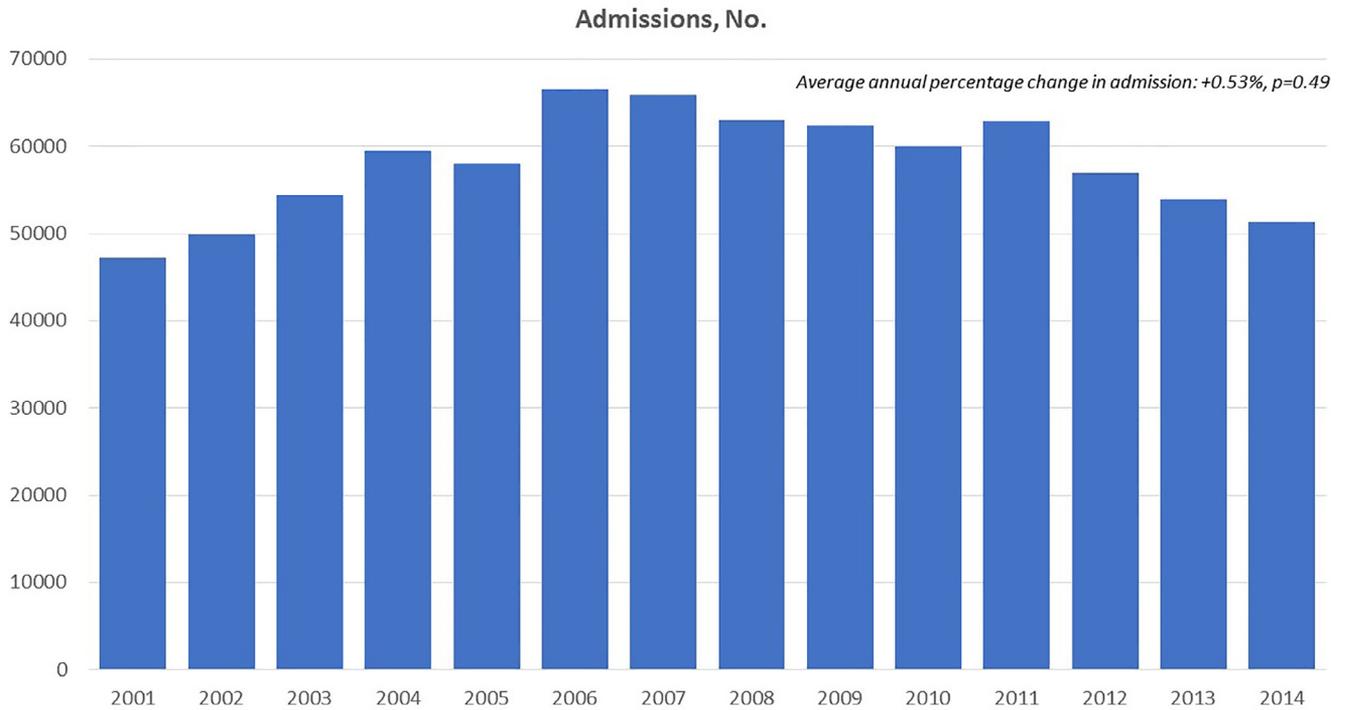


Fig. 1. Trend in primary heart failure admissions among end-stage renal disease patients in the US.

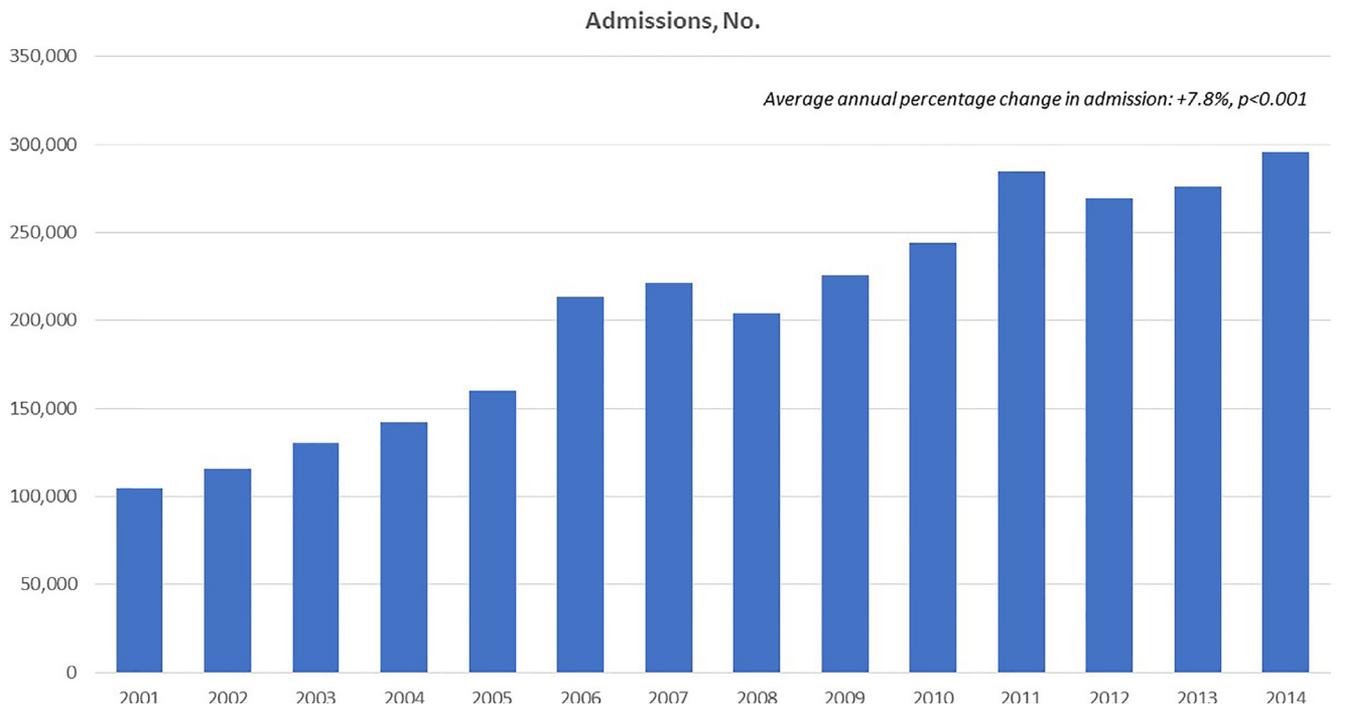


Fig. 2. Trend in secondary heart failure admissions among end-stage renal disease patients in the US.

mortality was higher among patients aged ≥ 65 years compared with those aged <65 years (odds ratio [OR] 2.4, 95% confidence interval [CI] 2.2–2.6; $P < .001$; Supplemental Fig. 1), with similar rates of decline in mortality for hemodialysis (-3.7% ; $P < .001$) and those ≥ 65 years (-3.0% ; $P < .001$). Among patients on peritoneal dialysis, mortality was

significantly higher than among patients on hemodialysis (OR 1.42, 95% CI 1.15–1.75; $P = .001$, Supplemental Fig. 2), with higher rates of decline in mortality for hemodialysis than for peritoneal dialysis (hemodialysis -5.3% [$P < .001$], peritoneal dialysis -4.6% [$P = .02$]). Women had significantly lower risk of mortality than men (OR 0.75,

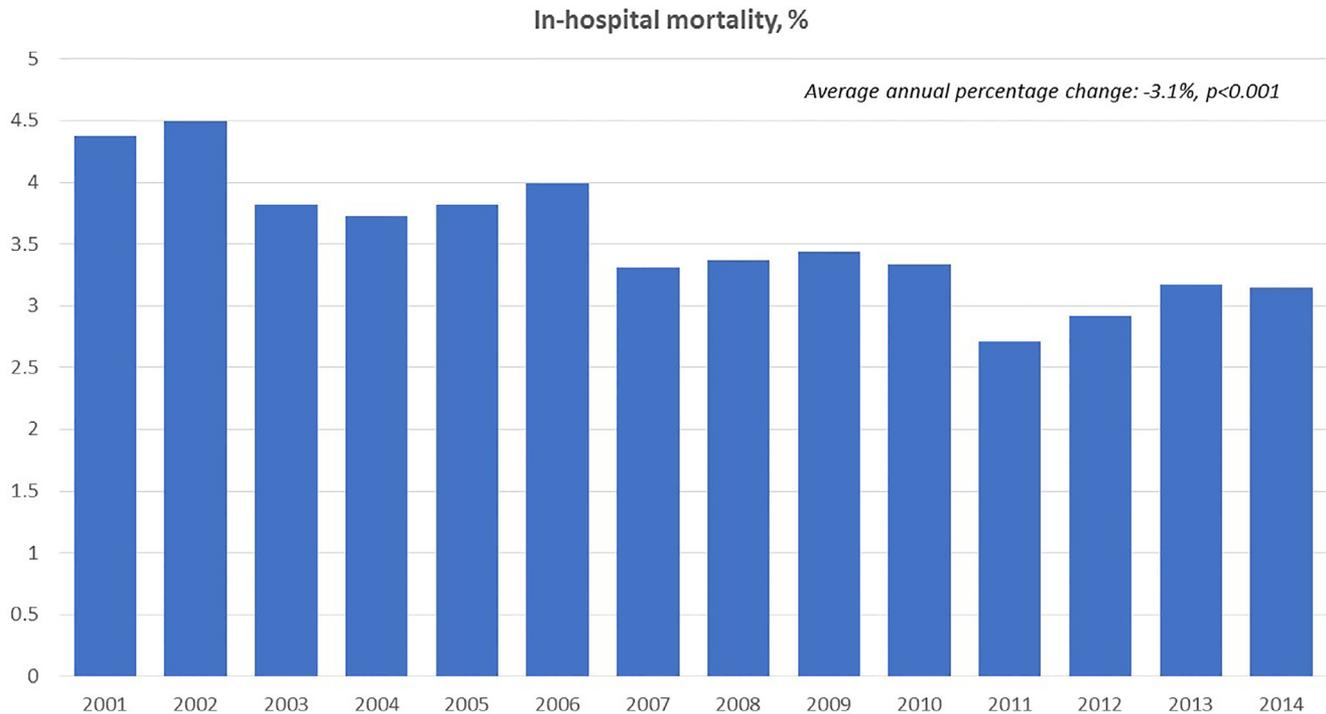


Fig. 3. Trend in in-hospital mortality among end-stage renal disease patients hospitalized with primary heart failure diagnosis in the US. Potential confounding variables including patient-level and hospital-level characteristics and socioeconomic status (Table 1) were adjusted for.

95% CI 0.70–0.80; $P < .001$; Supplemental Fig. 3) and higher rate of decline in mortality (men $-2.5%$ [$P < .001$], women $-4.1%$ [$P < .001$]). Finally, whites had higher mortality compared with other races (Supplemental Fig. 4). We found a declining trend across all races, but the average annual rate of decline was highest among Asians ($-7.1%$; $P < .001$) and lower among blacks ($-2.8%$; $P < .001$). The length of stay (LOS) decreased from 6.25 days in 2001 to 5.08 days in 2014 ($P < .001$; Fig. 4) with the lowest LOS reported in 2011 (4.98 days) (Fig. 4). The trends of LOS, categorized in different eras, are presented in Supplemental Table 2. Nonroutine discharge increased steadily from 28.65% in 2001 to 38.67% in 2014, with an average annual percentage change of $+3.3%$ ($P < .001$; Fig. 5). Approximately 80% of patients were discharged home (14.42% required home health services) and 16.71% were transferred to an extended-care facility after discharge (Supplemental Fig. 5). Finally, the average annual hospitalization cost varied from \$7972 in 2001 to \$8162 in 2014, with a decreasing trend from 2011 to 2014. An average annual change of $-\$280$ from \$10,160 in 2001 to \$8307 in 2014 ($P = .004$) was found among ESRD patients requiring peritoneal dialysis (Fig. 6). Median cost was significantly higher among ESRD patients on peritoneal dialysis compared with hemodialysis (mean difference in cost \$2295, 95% CI \$1520–\$3070; $P < .001$; Fig. 6).

Among ESRD patients admitted with a secondary HF diagnosis, in-hospital mortality declined significantly from 2001 to 2014, with an average annual percentage change of $-2.6%$ ($P < .001$; Fig. 7). In-hospital mortality was higher

among patients aged ≥ 65 years compared with those aged < 65 years (OR 2.0, 95% CI 1.97–2.1; $P < .001$), with similar rates of decline in patients < 65 years ($-2.1%$; $P < .001$) and those ≥ 65 years ($-3.0%$; $P < .001$). Women had significantly lower risk of mortality than men (OR 0.87, 95% CI 0.85–0.9; $P < .001$) and similar rates of decline in mortality ($-2.6%$; $P < .001$ for both). Finally, whites and Asians had higher mortality compared with blacks and Hispanics with a similar declining trend across all races. The LOS decreased from 9.15 days in 2001 to 7.67 days in 2014 ($P < .001$; Supplemental Fig. 6). Nonroutine discharge increased during the study period with an average annual percentage change of $+1.5%$ ($P < .001$; Supplemental Fig. 7). Approximately one-half of the patients were discharged home (16.8% required home health services) and 28.8% were transferred to an extended-care facility after discharge. Finally, the average annual hospitalization cost among patients on hemodialysis varied from \$12,167 to \$13,925 from 2001 to 2011 and decreased to \$12,118–\$12,238 in the years 2012–2014 (Supplemental Fig. 8). Although in-hospital mortality was slightly higher in peritoneal dialysis than in hemodialysis patients admitted with a secondary HF diagnosis (OR 1.14, 95% CI 1.07–1.22; $P < .001$), we did not identify differences in hospitalization cost among between the 2 groups.

Discussion

The salient findings of this analysis of a nationally representative sample of hospital admissions can be summarized

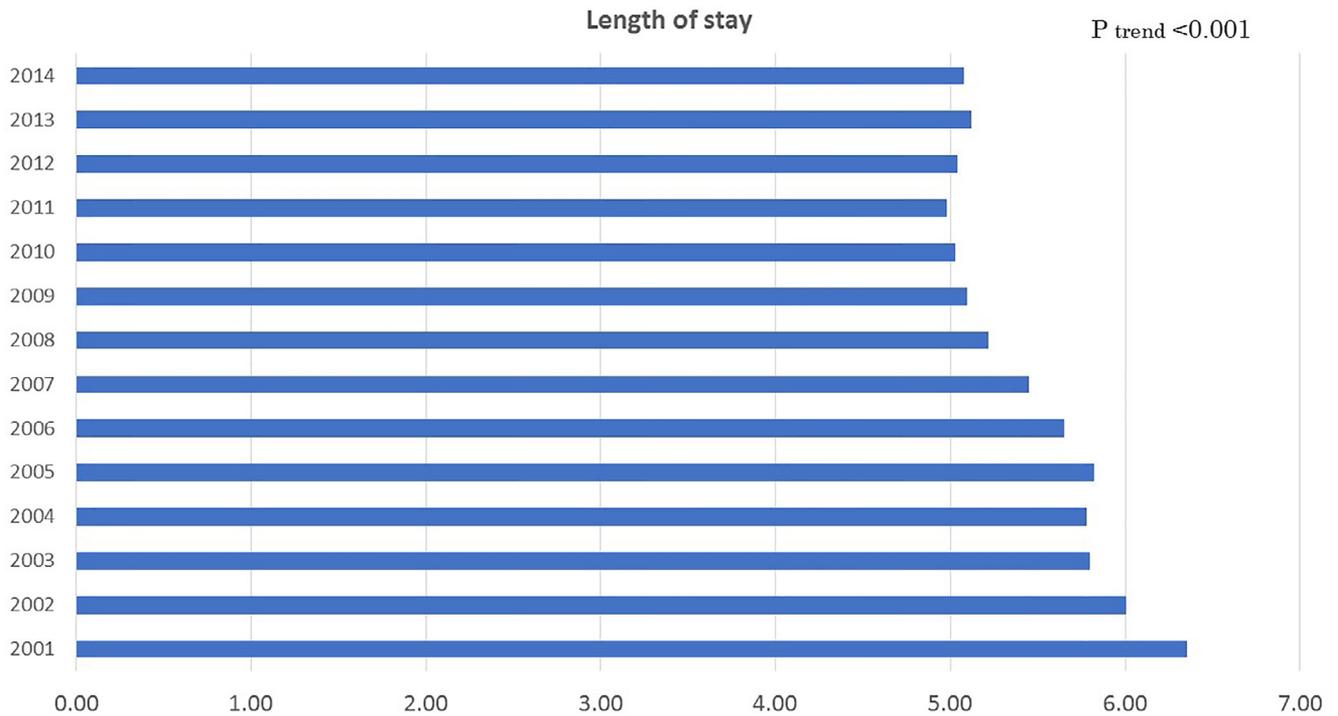


Fig. 4. Trend in length of stay among end-stage renal disease patients hospitalized with a primary heart failure diagnosis. Analyses were adjusted for patient-level and hospital-level characteristics and socioeconomic status.

as follows: (1) Among ESRD patients on dialysis, primary HF admissions peaked in 2006 and gradually declined after that, whereas secondary HF admissions increased from 2001 to 2014; (2) the comorbidity prevalence of these

patients increased during the study period and can explain the increase in secondary HF admissions; (3) in-hospital mortality declined significantly for patients admitted with primary or secondary HF diagnosis and was higher for men,

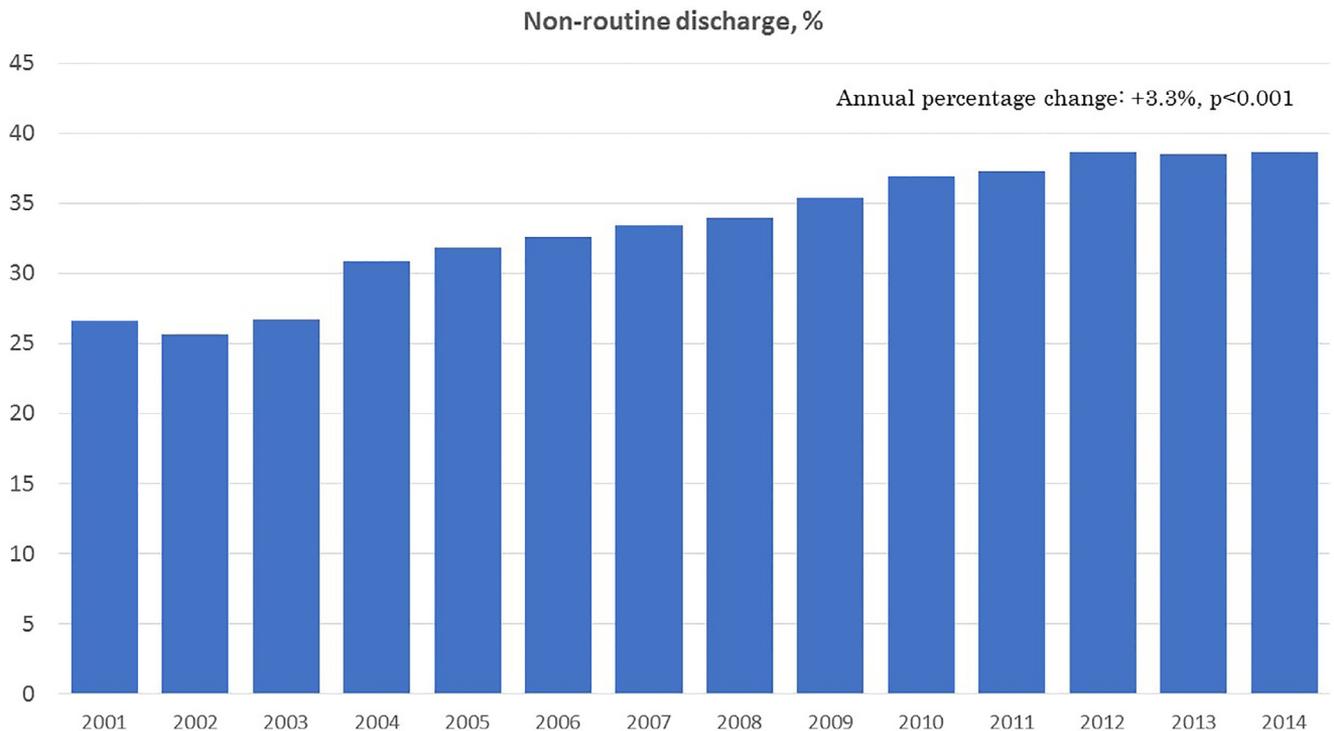


Fig. 5. Trend in nonroutine discharge after primary heart failure hospitalization among end-stage renal disease patients. Analyses were adjusted for patient-level and hospital-level characteristics and socioeconomic status.

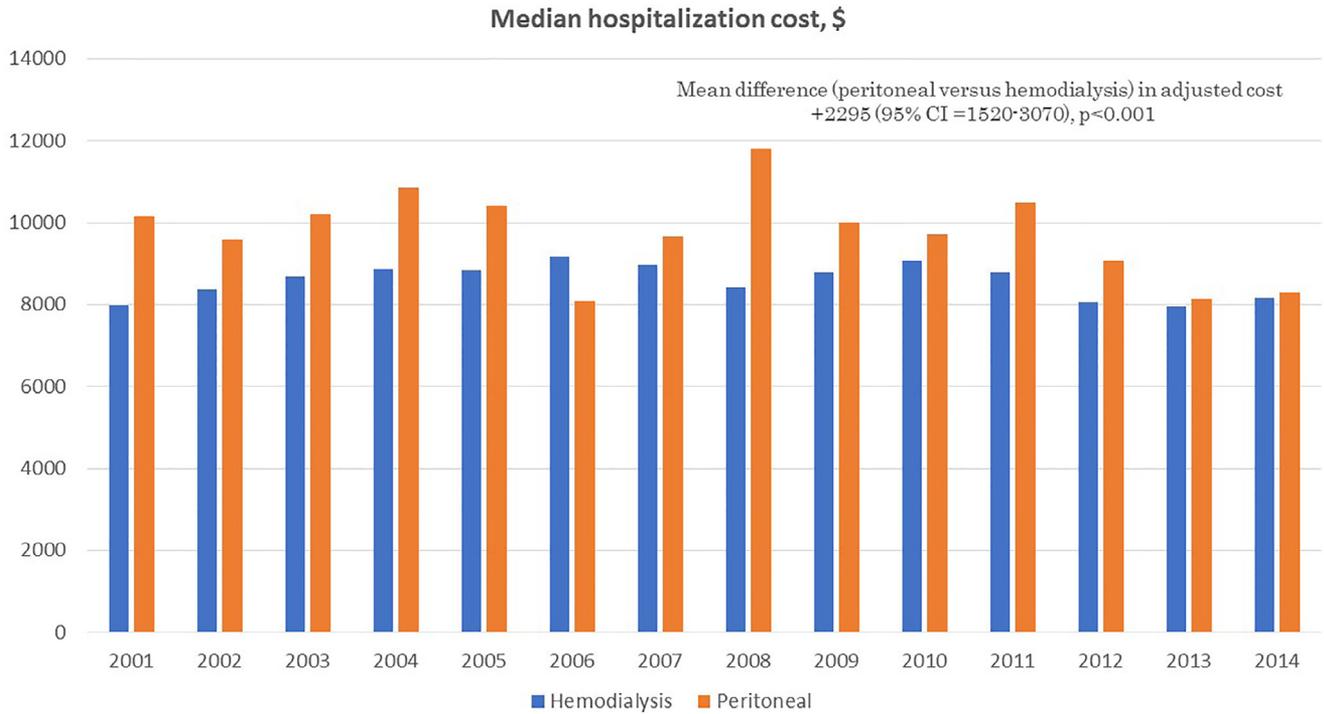


Fig. 6. Trend in cost of primary heart failure admissions among end-stage renal disease patients. Analyses were adjusted for patient-level and hospital-level characteristics and socioeconomic status.

whites, and patients ≥ 65 years; (4) LOS of primary and secondary HF admissions decreased significantly; and (5) although the number of nonroutine hospital discharges increased, the majority of patients were discharged home.

Cardiac disease is responsible for as many as one-half of the deaths in dialysis patients.⁸ In ESRD patients, cardiac dysfunction ranges from left ventricular hypertrophy and left ventricular dilation to asymptomatic systolic dysfunction and

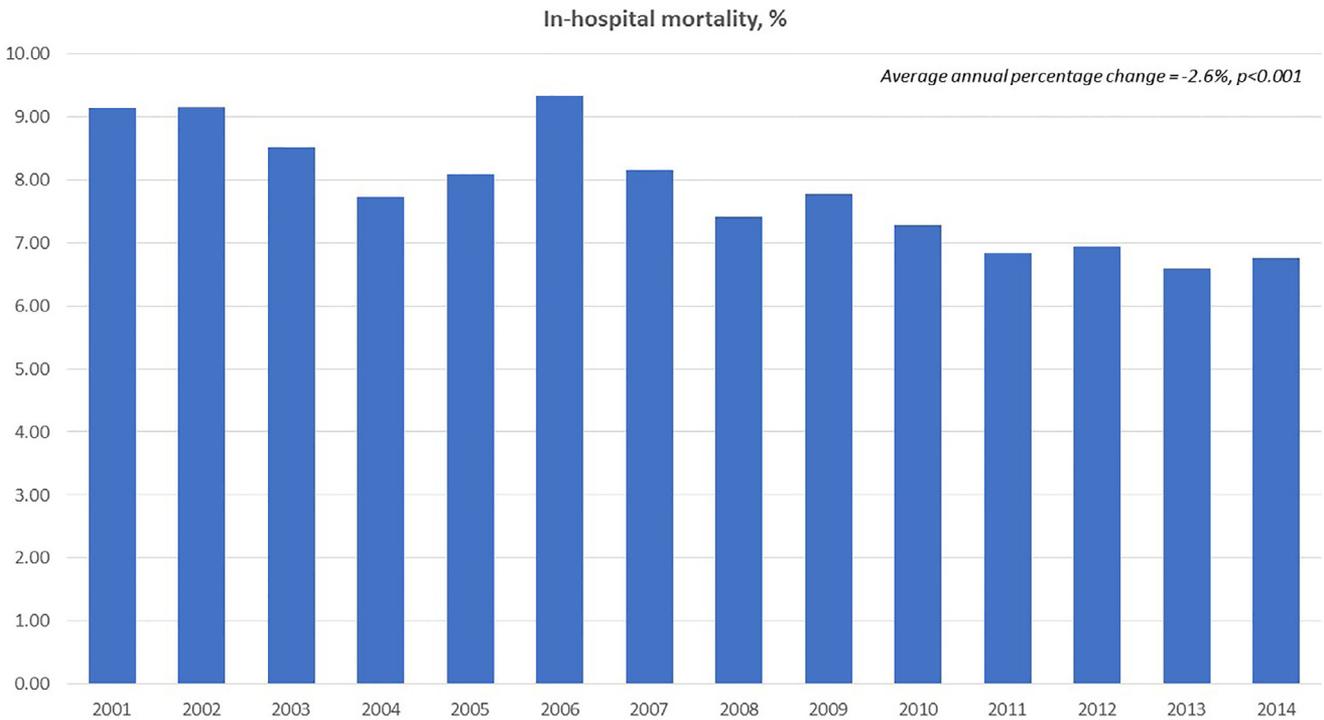


Fig. 7. Trend in in-hospital mortality among end-stage renal disease patients hospitalized with secondary heart failure diagnosis in the US. Potential confounding variables including patient-level and hospital-level characteristics and socioeconomic status (Supplemental Table 1) were adjusted for.

eventually symptomatic HF in sicker elderly patients with higher prevalence of comorbidities. Myocardial fibrosis and hypertrophy with or without ischemic heart disease is a frequent pathologic finding and a strong predictor of mortality.²² Therefore, in these patients there is a shift from ischemic to nonischemic etiologies of cardiac death.²³ The presence of HF is a strong predictor of mortality in both ESRD and non-ESRD patients. According to an analysis of the United States Renal Data System of 310,456 incident hemodialysis patients with a first hospital admission for HF or fluid overload, 5-year survivals were only 12.5% and 20.2%, respectively.²⁴ Mortality during the index hospital admission was 8.7%, which is higher than the in-hospital mortality found in our analysis. Patients with HF were older, more often white, and more likely to have diabetes or hypertension.²⁴ As confirmed in our analysis, comorbid conditions are more prevalent in new patients started on dialysis today than in previous years.^{25,26} The presence of coronary artery disease can explain why age and male sex are significant predictors of mortality. The finding of lower survival among white patients can be explained by increased mortality in sicker black patients before starting dialysis or by different causes of cardiomyopathy in black patients (more hypertensive than ischemic cardiomyopathy). However, the main finding of our analysis is the gradual decline of in-hospital mortality across all age, sex, and race subgroups.

A decline in long-term mortality has been noted in previous studies^{27–29} and is related in part to higher intensity of dialysis. Most importantly, there is a reported trend toward improved adherence to guideline-directed medical therapies and scheduled follow-ups among ESRD patients with HF.¹⁶ As previously reported by our group, among all patients hospitalized with HF, HF admission and in-hospital mortality rates declined significantly after 2005 and these improvements coincided with the publication of the 2005 ACC/AHA HF guidelines.²¹ Despite the lack of data from randomized clinical trials supporting the safety and efficacy of HF therapies in patients with ESRD, the National Kidney Foundation Kidney Disease Outcomes Initiative work group guidelines recommend angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB) and β -blockers for all ESRD patients with symptomatic HF who are receiving dialysis and who have HF with a reduced ejection fraction (HFrEF),³⁰ based on findings from smaller clinical trials that demonstrated improved outcomes with the use of ACEi/ARB and β -blockers.^{31–33} A retrospective analysis of the Get With The Guidelines—HF study participants who were admitted with primary HF diagnosis demonstrated a temporal increase in adherence to ACEi/ARBs, β -blockers, and early postdischarge follow-up among dialysis patients that approached 90% by the end of the study period.¹⁶ However, adherence to quality measures did not have a meaningful impact on 1-year survival and readmission rates. Several factors, including high prevalence of comorbid conditions, prescription of complex drug regimens with high risk for nonadherence, poor tolerance to ACEi, ARBs, or β -blockers because of intradialytic hypotension or hyperkalemia, may explain this discordance

between adherence to HF quality measures and poor long-term outcomes. Furthermore, in-hospital utilization of guideline-directed medical therapies remains low compared with patients not requiring dialysis.³⁴ Because the NIS does not provide information on medications use, the association between prescription patterns of guideline-directed medical therapies and outcomes in HF patients with dialysis remains to be determined.

Although, ESRD patients admitted with primary or secondary HF diagnosis had an increasing prevalence of comorbidities, LOS decreased and hospitalization cost did not change substantially during the study period. These observations may be explained by improvement in adherence to quality measures, better volume and afterload control, and early recognition and treatment of comorbidities, which resulted in improved mortality rates and LOS. Furthermore, it is possible that patients are being provided with initial care in the hospital and once they are stable their care is transferred to outpatient dialysis centers with a close follow-up that includes a physician visit. The increase in the nonroutine discharges could also reflect the increasing prevalence of comorbidities in this population. Finally, we found higher in-hospital mortality and cost to be associated with the use of peritoneal dialysis. These observations are in line with earlier studies that suggested worse survival among ESRD with HF likely because of poor volume control.³⁵

Study Limitations

Potential limitations of the study should be considered when interpreting the results. Coding inaccuracies leading to incomplete or misclassified documentation, absence of data on HFrEF versus HF with preserved ejection fraction, and lack of useful clinical variables such as medications, laboratory data, and long-term clinical outcomes are some of the inherent limitations of this administrative database. Furthermore, the NIS provides number of hospitalizations rather than unique patients, and the hospitalizations reported here represent a composite of both first admission (during the study period) and readmissions. Also, the number of certain patient populations, such as those on peritoneal dialysis, was small and the findings of our analysis should be interpreted with caution in the context of limited sample size. Finally, this database does not provide granular information regarding drug prescriptions and details of dialyses. Despite these limitations, the NIS captures a large sample size representative of the nationwide population of ESRD patients, and its analysis provides reliable estimates of in-hospital outcome trends.

Conclusion

Among ESRD patients on dialysis hospitalized with HF from 2001 to 2014, in-hospital mortality and length of stay improved despite an increase in comorbidity prevalence. Adherence to guideline-directed medical and device therapies, along with maximum tolerated volume and afterload reduction and early evaluation of candidacy for kidney

transplantation, can lead to improved outcomes despite high comorbidity prevalence among ESRD patients with HF. Further prospective studies are warranted to examine the specific effects of each of the available therapeutic measures on outcomes of HF patients with ESRD.

Disclosures

None.

Supplementary materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.cardfail.2019.02.020>.

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