Biomarkers

Length of stay and readmission in older adults hospitalized for heart failure

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Abstract

Introduction: Hospital length of stay (LoS) and hospital readmissions are metrics of healthcare performance. We examined the association between these two metrics in older patients hospitalized with decompensated heart failure (HF).

Material and methods: Eight thousand and forty-nine patients hospitalized for HF in 106 U.S. hospitals had a median LoS of 5 days; among them, 3777 had a LoS > 5 days. Using propensity scores for LoS > 5 days, we assembled 2723 pairs of patients with LoS 1-5 vs. > 5 days. The matched cohort of 5446 patients was balanced on 40 baseline characteristics. We repeated the above process in 7045 patients after excluding those with LoS > 10 days, thus assembling a second matched cohort of 2399 pairs of patients with LoS 1-5 vs. 6-10 days. Hazard ratios (HR) and 95% confidence intervals (CI) for outcomes associated with longer LoS were estimated in matched cohorts.

Results: In the primary matched cohort (n = 5446), LoS > 5 days was associated with a higher risk of all-cause readmission at 30 days (HR = 1.16; 95% CI: 1.04–1.31; p = 0.010), but not during longer follow-up. A longer LoS was also associated with a higher risk of mortality during 8.8 years of follow-up (HR = 1.13; 95% CI: 1.06–1.21; p < 0.001). LoS had no association with HF readmission. Similar associations were observed among the matched sensitivity cohort (n = 4798) that excluded patients with LoS > 10 days.

Conclusions: In propensity score-matched balanced cohorts of patients with HF, a longer LoS was independently associated with poor outcomes, which persisted when LoS > 10 days were excluded.

Key words: length of stay, 30-day all-cause readmission, heart failure, all-cause mortality.

Introduction

Heart failure (HF) is the leading cause for 30-day all-cause readmission among older patients in the United States [1], the reduction of which is a focus of the Affordable Care Act, the 2010 comprehensive health care reform law [2]. Hospitals, on the other hand, are also en-

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Cherinne Arundel MD Washington DC VA Medical Center 50 Irving St NW, Washington DC 20422, USA Phone: 1-202-745-8386 E-mail: Cherinne.Arundel@ va.gov couraged by the Medicare Inpatient Prospective Payment System to have a shorter length of stay (LoS) [3, 4], which has been shown to be variously associated with outcomes [5–7]. In the current study, we examined the association between LoS and hospital readmission, two metrics of healthcare performance, in a propensity score-matched cohort of hospitalized patients with HF.

Material and methods

Data source and study population

Data for the study were collected from the Alabama Heart Failure Project, a registry of Medicare beneficiaries hospitalized for HF in the state of Alabama, the details of which have been previously published [8–10]. Briefly, extensive baseline data were collected on 8555 discharged patients from 106 Alabama hospitals during 1998–2001 with a principal discharge diagnosis of HF[11–13]. Medicare beneficiaries are the recipients of the United States government program called Medicare that provides health care coverage to American citizens 65 years or older, and to certain younger people with disability or permanent kidney failure requiring dialysis or a transplant [14].

Study variables

Data on baseline characteristics including comorbidities, medications, laboratory, and in-hospital events were collected by chart abstraction. Our exposure variable was LoS, which was calculated by subtracting the date of admission from the date of discharge. Of the 8049 patients discharged alive, 3777 had longer than median LoS of 5 days (25–75 percentile, 4–8 days; 5–95 percentile, 2–15 days; 1–99 percentile, 2–25 days; Figure 1). Our outcome variables included all-cause readmission, HF readmission, all-cause mortality, and the combined endpoint of all-cause readmission or mortality. All outcomes were examined at 30 days, 12 months, and during the overall 8.8 (median = 2.5) years of follow-up. Information on outcome events and times to those events were obtained from the Medicare data files [8].

Assembly of a balanced study cohort

We assembled a primary propensity scorematched cohort in which patients with a longer and a shorter LoS would be balanced on key measured baseline characteristics [15-17]. We estimated propensity scores for LoS > 5 days for each of the 8049 patients using a logistic regression model based on 40 baseline characteristics displayed in Figure 2 [17, 18]. We then used a greedy matching protocol to match 2723 patients with LoS > 5 days with another 2723 patients who had LoS of 1–5 days and similar propensity scores, thus assembling a matched cohort of 5446 patients (Figure 1) [19, 20].

Assembly of a balanced sensitivity cohort

To determine whether the results of the study could be replicated after excluding a potentially sicker cohort of patients with long LoS, we repeat-

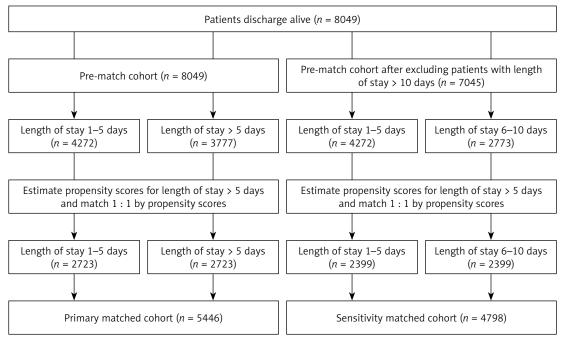


Figure 1. Flow chart displaying assembly of primary matched cohort of patients with heart failure by hospital length of stay 1–5 versus > 5 days and sensitivity matched cohort of patients with heart failure by hospital length of stay 1–5 versus 6–10 days

ed the above process in 7045 patients after excluding those with LoS > 10 days. Of these, 2773 had LoS 6–10 days (Figure 1). The assembled second sensitivity matched cohort of 2399 pairs of patients with LoS 1–5 vs. 6–10 days was also balanced on 40 baseline characteristics.

Statistical analyses

Pearson χ^2 and Wilcoxon rank-sum tests were used for descriptive analyses to compare between-group differences in baseline characteristics as appropriate. Kaplan-Meier survival plots for all-cause mortality by the two LoS categories during the overall follow-up of 8.8 (median = 2.5) years were generated using the primary matched data. Cox regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for outcomes associated with longer LoS in both matched cohorts. We also examined the association of LoS with the primary outcome among the 8049 pre-match patients using Cox regression models, separately adjusting for propensity scores and the 40 variables used to estimate propensity scores. We then fitted restricted cubic spline models with 4 knots at 3, 5 (reference), 7 and 10 days to assess nonlinearity of the relationship of LoS with mortality during 8.8 (median = 2.5) years of follow-up.

To examine whether significant associations observed in our matched data could be explained away by an unmeasured baseline characteristic, we conducted formal sensitivity analyses using Rosenbaum's approach [21]. From the 2723 pairs of matched patients, we identified pairs in which we could directly compare survival times within the pair to determine whether one member of the pair clearly had a longer survival or event-free survival than the other member. We then used the sign-score test to calculate "sensitivity bounds" for a hypothetical unmeasured confounder to determine how much it would need to increase the odds of having a longer LoS to explain away any significant association between LoS and outcomes. A significant sign-score test provides strong evidence of a relationship between longer LoS and time to death. Our sensitivity analysis assumes that the potential unmeasured confounder is a binary baseline characteristic that is a near perfect predictor of the outcomes and also not strongly correlated with any of the 40 baseline characteristics used in our propensity score model. However, sensitivity analysis cannot determine whether such an unmeasured confounder exists. All statistical tests were two-tailed with a *p*-value < 0.05 considered significant. IBM SPSS Statistics for Windows, Version 25 (IBM Corp. Armonk, NY) and SAS version 9.4 (SAS Institute Inc., Cary, NC) were used for data analyses.

Results

Baseline characteristics

Patients in our propensity score-matched cohort (n = 5446) had a mean age of 75.8 ±10.8 years, 58% were female, and 25% were African American. Prior to matching, HF patients with LoS > 5 days were older and had a higher prevalence of comorbidities and in-hospital events (Table I). Post-match absolute standardized differences were < 10% for all 40 measured baseline characteristics, suggesting no residual consequential imbalance between the two LoS groups (Figure 2). After matching, patients in the sensitivity cohort were also balanced on all 40 measured baseline characteristics.

Length of stay and readmission in the matched primary cohort

30-day all-cause readmission occurred in 20% and 23% of matched patients with LoS 1-5 and > 5 days, respectively (hazard ratio (HR) = 1.16; 95% confidence interval (CI): 1.04–1.31; *p* = 0.010; Table II). Findings from our sensitivity analyses demonstrate that the significant associations of LoS > 5 days and 30-day all-cause readmission were insensitive to unmeasured confounders. Of the 2723 matched pairs, in 965 pairs we were able to determine which patient within a matched pair had a shorter 30-day total readmission-free survival, and in 55% (528/965) of those pairs, they belonged to the longer LoS group (sign-score test p = 0.003). A hidden baseline characteristic would need to increase the odds of having a longer LoS by 6%. HR (95% CI) for 30-day all-cause readmission associated with LoS as a continuous variable in the matched data was 1.02 (1.01–1.04; *p* < 0.001).

In the pre-match cohort, multivariable-adjusted and propensity score-adjusted HRs (95% Cls) for 30-day all-cause readmission associated with LoS > 5 days were both 1.19 (1.07–1.32; p = 0.001). LoS had no association with 30-day HF readmission. Associations of a longer LoS and all-cause readmission at 12 months and during 8.8 (median = 2.5) years of follow-up are displayed in Table II.

30-day HF readmission occurred in 7% and 8% of matched patients with LoS 1–5 and > 5 days, respectively (HR = 1.12; 95% CI: 0.92–1.35; p = 0.266; Table II). There was no association with HF readmission during longer follow-up.

Length of stay and all-cause mortality in the matched primary cohort

30-day all-cause mortality occurred in 5% and 7% of matched patients with LoS 1–5 and > 5 days, respectively (HR = 1.41; 95% CI: 1.12-1.76;

Parameter	Before pro	pensity score	matching	After propensity score matching		
	Lengt	n of stay (n =	8049)	Lengt	n of stay (n =	5446)
	1–5 days (n = 4272)	> 5 days (n = 3777)	<i>P</i> -value	1–5 days (n = 2723)	> 5 days (n = 2723)	<i>P</i> -value
Age [years]	75 ±11	76 ±11	< 0.001	76 ±11	76 ±11	0.911
Female	2407 (56)	2220 (59)	0.028	1577 (58)	1594 (59)	0.640
African American	1070 (25)	924 (25)	0.545	680 (25)	675 (25)	0.875
Admission from nursing home	248 (6)	297 (8)	< 0.001	186 (7)	181 (7)	0.787
Left ventricular ejection fraction:			< 0.001			0.947
< 45%	1496 (35)	1571 (42)		1064 (39)	1060 (39)	
≥ 45%	1162 (27)	1250 (33)		852 (31)	863 (32)	
Unknown	1614 (38)	956 (25)		807 (30)	800 (29)	
Past medical history:						
Smoking history	529 (12)	393 (10)	0.005	285 (11)	304 (11)	0.407
Prior heart failure	3025 (71)	2787 (74)	0.003	1972 (72)	1962 (72)	0.762
Hypertension	2942 (69)	2676 (71)	0.053	1902 (70)	1903 (70)	0.976
Coronary artery disease	2313 (54)	2095 (56)	0.234	1479 (54)	1471 (54)	0.828
Diabetes mellitus	1792 (42)	1707 (45)	0.003	1201 (44)	1191 (44)	0.785
Stroke	791 (19)	865 (23)	< 0.001	564 (21)	559 (21)	0.867
COPD	1393 (33)	1462 (39)	< 0.001	988 (36)	962 (35)	0.462
Dementia	356 (8)	396 (11)	0.001	239 (9)	242 (9)	0.886
Cancer	74 (2)	94 (3)	0.018	59 (2)	54 (2)	0.635
Atrial fibrillation	955 (22)	1171 (31)	< 0.001	732 (27)	736 (27)	0.903
LBBB	567 (13)	512 (14)	0.710	369 (14)	365 (13)	0.874
Clinical and laboratory findings:						
Pulse [beats per minute]	88 ±22	91 ±23	< 0.001	90 ±22	90 ±23	0.795
Systolic blood pressure [mm Hg]	152 ±33	146 ±32	< 0.001	149 ±32	149 ±33	0.738
Pulmonary edema by chest X-ray	2725 (64)	2739 (73)	< 0.001	1850 (68)	1889 (69)	0.255
Serum creatinine [mEq/l]	1.58 ±1.4	1.64 ±1.2	0.035	1.62 ±1.4	1.60 ±1.2	0.672
In hospital events:						
Pneumonia	777 (18)	1271 (34)	< 0.001	662 (24)	657 (24)	0.874
Acute myocardial infarction	121 (3)	217 (6)	< 0.001	101 (4)	99 (4)	0.885
Pressure ulcer	186 (4)	493 (13)	< 0.001	176 (7)	175 (6)	0.956
Hospital and care characteristics:						
Rural hospital	1548 (36)	964 (26)	< 0.001	822 (30)	788 (29)	0.313
Cardiology care	1887 (44)	2284 (61)	< 0.001	1473 (54)	1482 (54)	0.807
Intensive care	45 (1)	267 (7)	< 0.001	45 (2)	45 (2)	1.000
Home health care	561 (13)	853 (23)	< 0.001	468 (17)	458 (17)	0.718
Hospice	54 (1)	128 (3)	< 0.001	49 (2)	53 (2)	0.689
Admission medications:						
ACE inhibitors and ARB	2157 (51)	1704 (45)	< 0.001	1268 (47)	1296 (48)	0.447
β-Blockers	1277 (30)	1020 (27)	0.004	764 (28)	777 (29)	0.696
Loop diuretics	2733 (64)	2558 (68)	< 0.001	1793 (66)	1805 (66)	0.731
Digoxin	1545 (36)	1351 (36)	0.711	985 (36)	968 (36)	0.631
Potassium sparing diuretics	279 (7)	299 (8)	0.016	194 (7)	190 (7)	0.832
Potassium supplements	1595 (37)	1471 (39)	0.138	1056 (39)	1044 (38)	0.738

Table I. Baseline characteristics by length of stay, before and after propensity score matching

Parameter	Before propensity score matching Length of stay (n = 8049)			After propensity score matching		
				Length of stay (n = 5446)		
	1-5 days (n = 4272)	> 5 days (n = 3777)	<i>P</i> -value	1–5 days (n = 2723)	> 5 days (n = 2723)	<i>P</i> -value
Discharge medications:						
ACE inhibitors and ARB	2631 (62)	2104 (56)	< 0.001	1614 (59)	1622 (60)	0.825
β-Blockers	1325 (31)	1111 (29)	0.119	814 (30)	829 (30)	0.658
Loop diuretics	3460 (81)	3059 (81)	0.998	2212 (81)	2230 (82)	0.529
Digoxin	1741 (41)	1674 (44)	0.001	1172 (43)	1167 (43)	0.891
Potassium sparing diuretics	534 (13)	609 (16)	< 0.001	386 (14)	386 (14)	1.000
Potassium supplements	2011 (47)	1667 (44)	0.008	1258 (46)	1245 (46)	0.724

Table I. Cont.

Results presented as n (%) or mean (± SD).

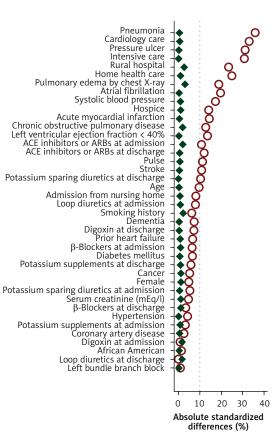
p = 0.003; Table II). Of the 2723 matched pairs, in 289 pairs we were able to determine which patient within a matched pair had a shorter 30-day survival, and in 55% (169/289) of those pairs, they belonged to the longer LoS group (sign-score test p = 0.004). A hidden baseline characteristic would need to increase the odds of having a longer LoS by 12%. HR (95% CI) for 30-day all-cause mortality associated with LoS as a continuous variable in the matched data was 1.05 (95% Cl: 1.03–1.07; p < 0.001). The association of a longer LoS with all-cause mortality was attenuated during longer follow-up, but remained significant both at 12 months (HR = 1.16; 95% CI: 1.06–1.27; p = 0.002) and during the overall (8.8 years; median = 2.5 years) follow-up (HR = 1.13; 95% CI: 1.06–1.21; p < 0.001; Table II and Figure 3). Of the 2723 matched pairs, in 2417 (89%) pairs we were able to determine which patient within a matched pair had a shorter overall survival, and in 54% (1293/2417) of those pairs, they belonged to the longer LoS group (sign-score test p < 0.001). A hidden baseline characteristic would need to increase the odds of having a longer LoS by 6%.

Findings from our restricted cubic spline analysis demonstrated that LoS > 10 days is associated with a significantly higher risk for overall all-cause mortality and that there is no evidence that this association is nonlinear (*p* for test of non-linearity, > 0.20 and 0.07 in the matched and pre-match data, respectively (Figure 4). In the pre-match cohort, multivariable-adjusted and propensity score-adjusted HRs (95% Cls) for 30-day all-cause mortality associated with LoS > 5 days were 1.44 (1.17–1.77; *p* = 0.001) and 1.40 (1.14–1.72; *p* = 0.001), respectively.

Findings from the matched sensitivity cohort

30-day all-cause readmission occurred in 20% and 22% of matched patients with LoS 1–5 and 6–10 days, respectively (HR = 1.15; 95% CI: 1.02–

1.30; p = 0.026; Table III). 30-day all-cause mortality occurred in 5% and 6% of matched patients with LoS 1–5 and 6–10 days, respectively (HR = 1.32; 95% CI: 1.03–1.68; p = 0.027; Table III). The associations of LoS with other outcomes in the matched sensitivity cohort are displayed in Table III.



Post-match
 O Pre-match

Figure 2. Love plot displaying absolute standardized differences for 40 baseline characteristics between heart failure patients with hospital length of stay 1–5 versus > 5 days, before and after propensity score matching

ACE – angiotensin-converting enzyme, ARB – angiotensin receptor blockers.

Parameter	Length	of stay	Hazard ratios associated		
-	1–5 days (n = 2723)	>5 days (n = 2723)	 with longer length of stay (95% confidence intervals) 		
30-day outcomes:					
All-cause readmission	20% (536)	23% (614)	1.16 (1.04–1.31); <i>p</i> = 0.010		
Heart failure readmission	7% (200)	8% (221)	1.12 (0.92–1.35); <i>p</i> = 0.266		
All-cause mortality	5% (127)	7% (177)	1.41 (1.12–1.76); <i>p</i> = 0.003		
All-cause readmission or mortality	23% (627)	26% (717)	1.16 (1.04–1.29); <i>p</i> = 0.006		
12-month outcomes:					
All-cause readmission	66% (1803)	67% (1819)	1.06 (0.99–1.13); <i>p</i> = 0.082		
Heart failure readmission	32% (866)	32% (860)	1.04 (0.94–1.14); <i>p</i> = 0.471		
All-cause mortality	30% (827)	34% (923)	1.16 (1.06–1.27); <i>p</i> = 0.002		
All-cause readmission or mortality	76% (2058)	77% (2086)	1.06 (1.00–1.13); <i>p</i> = 0.046		
Overall (8.8 years) outcomes:					
All-cause readmission	86% (2351)	86% (2327)	1.04 (0.98–1.10); <i>p</i> = 0.232		
Heart failure readmission	57% (1557)	56% (1523)	1.05 (0.98–1.13); <i>p</i> = 0.178		
All-cause mortality	66% (1794)	70% (1903)	1.13 (1.06–1.21); <i>p</i> < 0.001		
All-cause readmission or mortality	97% (2643)	97% (2630)	1.04 (0.99–1.10); <i>p</i> = 0.146		

 Table II. Associations of length of stay with outcomes in a propensity score-matched cohort of 5446 hospitalized patients with heart failure

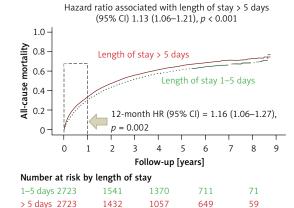


Figure 3. Kaplan Meier plot for all-cause readmission in 2723 pairs of propensity score-matched patients with heart failure by length of stay 1–5 versus > 5 days

Discussion

Findings from our study demonstrate that in older patients hospitalized for HF, a LoS > 5 days was associated with a higher risk of 30-day allcause readmission and all-cause mortality, but not with HF readmission. Further, only the association with all-cause mortality persisted during longer follow-up. We also observed that these findings persisted when we excluded patients with LoS > 10 days. These findings from rigorously assembled, propensity score-matched cohorts highlight the complex interplay between LoS and outcomes in older patients with HF.

A potential explanation for these associations include confounding by conditions and complications that may have necessitated the longer LoS [22, 23]. However, the findings of our study may not be explained by the subset of very sick patients with unusually long LoS, as we found similar results when we repeated our analysis after excluding those with LoS > 10 days. An examination of the baseline characteristics in the pre-match cohort demonstrated that patients in the longer LoS group had a lower mean blood pressure, and a higher prevalence of pre-admission comorbidities, admission pulmonary edema, and in-hospital complications, which have been shown to be associated with poor outcomes [24, 25]. These patients also had a lower prevalence of pre-admission use of ACE inhibitors and β -blockers, drugs known to improve outcomes [26, 27]. Although the distribution of these and other baseline characteristics was balanced after propensity score-matching, imbalanced unmeasured characteristics such as disease severity may act as confounders. For example, although the prevalence of pneumonia was similar after matching, it is possible that pneumonia in the longer LoS group was more severe or complicated. A longer LoS may also lead to

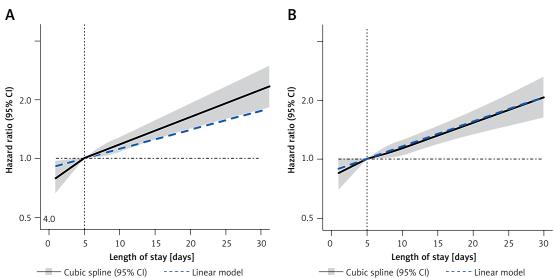


Figure 4. Restricted cubic spline regression analysis displaying risk of all-cause mortality during 8.8 (median = 2.5) years of follow-up by hospital length of stay in days as a continuous variable in patients with heart failure using 3 knots at length of stay 3, 5 (reference), 7 and 10 days. Solid black lines represent hazard ratios and shaded areas represent 95% confidence intervals. Plots on the left panel (**A**) are based on 8049 pre-match patients, adjusting for propensity scores, and those on the right panel (**B**) are based on 5446 propensity score-matched patients balanced on 40 baseline characteristics (non-linearity p > 0.2 for matched and 0.07 for pre-match patients)

Parameter	Length	of stay	Hazard ratios associated — with longer length of stay (95% confidence intervals)	
-	1–5 days (n = 2399)	6-10 days (n = 2399)		
30-day outcomes:				
All-cause readmission	20% (470)	22% (532)	1.15 (1.02–1.30); <i>p</i> = 0.026	
Heart failure readmission	7% (176)	8% (199)	1.14 (0.93–1.40); <i>p</i> = 0.200	
All-cause mortality	5% (113)	6% (148)	1.32 (1.03–1.68); <i>p</i> = 0.027	
All-cause readmission or mortality	23% (552)	26% (616)	1.14 (1.01–1.27); <i>p</i> = 0.030	
12-month outcomes:				
All-cause readmission	65% (1560)	67% (1602)	1.07 (1.00–1.15); <i>p</i> = 0.050	
Heart failure readmission	32% (770)	32% (777)	1.04 (0.94–1.15); <i>p</i> = 0.422	
All-cause mortality	30% (728)	33% (797)	1.13 (1.02–1.25); <i>p</i> = 0.019	
All-cause readmission or mortality	74% (1786)	76% (1829)	1.07 (1.00–1.14); <i>p</i> = 0.046	
Overall (8.8 years) outcomes:				
All-cause readmission	86% (2057)	86% (2055)	1.05 (0.99–1.12); <i>p</i> = 0.101	
Heart failure readmission	57% (1375)	57% (1365)	1.06 (0.99–1.14); <i>p</i> = 0.116	
All-cause mortality	66% (1581)	70% (1667)	1.12 (1.05–1.20); <i>p</i> = 0.001	
All-cause readmission or mortality	97% (2316)	97% (2314)	1.05 (0.99–1.11); <i>p</i> = 0.086	

Table III. Associations of length of stay with outcomes in a propensity score-matched cohort of 4798 hospitalized patients with heart failure that excluded those with length of stay > 10 days

a higher prevalence of unmeasured confounders such as loss of function, strength, coordination, and mobility [28, 29].

pitalized for HF [5–7]. Among 19,927 hospitalized patients with HF (2008–2011), compared with LoS 3–4 days, LoS 5–10 days was associated with a 17% higher risk of 30-day all-cause readmission and a 52% higher risk of 30-day all-cause mortal-

Several prior studies have examined the association of LoS with outcomes in patients hosity, but had no association with HF readmission [6]. The mean age of the patients in that study and their 30-day outcome rates are similar to those in our study [6]. However, our study is distinguished by the use of propensity score matching, which allowed us to achieve and display balance in key measured baseline characteristics between the two LoS groups. Taken together, these findings suggest that a longer LoS has a stronger association with mortality than with readmission. Future studies need to examine underlying reasons why a longer LoS may increase the risk of death, but not of readmission, and develop and test interventions that may improve post-discharge survival among the high-risk subset of patients with longer LoS.

Our study has several limitations. As in any observational study, bias due to an unmeasured confounder is possible. Although the management of heart failure with reduced ejection fraction has evolved, the findings of the current study are similar to those observed in a more contemporary population of HF patients [6]. Additionally, we had no data on brain natriuretic peptides, the use of vasodilators, sacubitril/valsartan, or inotropic drugs, and drug-drug interactions [30–34].

In conclusion, in older adults hospitalized for HF, when compared with a hospital length of stay of 1–5 days, a length of stay of 5–10 days is associated with a higher risk of both mortality and short-term readmission, but not with HF readmission.

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Prior presentations: Presented as an abstract at the American Heart Association meeting in 2015.

Conflict of interest

The authors declare no conflict of interest.

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