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Prior Heart Failure Hospitalization and Outcomes in Patients with Heart Failure with Preserved and Reduced Ejection Fraction

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Abstract

Background: A prior hospitalization due to heart failure is associated with poor outcomes in ambulatory patients with heart failure. Less is known about this association in hospitalized patients with heart failure and whether it varies by ejection fraction.

Methods: Of the 25,345 hospitalized patients in Medicare-linked OPTIMIZE-HF registry, 22,491 had known heart failure, of whom 7648 and 9558 had heart failure with preserved (≥50%) and reduced (≤40%) ejection fraction (HFpEF and HFrEF), respectively. Overall, 927 and 1862 patients with HFpEF and HFrEF had heart failure hospitalizations during six months before the index hospitalization, respectively. Using propensity scores for prior heart failure hospitalization, we assembled two matched cohorts of 924 pairs and 1844 pairs of patients with HFpEF and HFrEF, respectively, each balanced for 58 baseline characteristics. Cox regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for outcomes during six years of follow-up.

Results: Among 1848 matched patients with HFpEF, HRs (95% CIs) for all-cause mortality, all-cause readmission and heart failure readmission were 1.35 (1.21–1.50; p<0.001), 1.34 (1.21–1.47; p<0.001) and 1.90 (1.67–2.16; p<0.001), respectively. Respective HRs (95% CIs) in 3688

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matched patients with HFrEF were 1.17 (1.09 –1.26; p<0.001), 1.32 (1.23 –1.41; p<0.001), and 1.48 (1.37 –1.61; p<0.001).

Conclusions: Among hospitalized patients with heart failure, a prior heart failure hospitalization is associated with higher risks of mortality and readmission in both HFpEF and HFrEF. The relative risks of death and heart failure readmission appear to be higher in HFpEF than in HFrEF.

Keywords

Heart failure; Mortality; Prior hospitalization; Preserved ejection fraction; Readmission

Introduction

Heart failure hospitalization has been shown to be associated with poor outcomes in ambulatory younger patients with chronic heart failure, mostly among those with heart failure with reduced ejection fraction (HFrEF).[1–5] However, less is known about this association among hospitalized older patients with acute heart failure, in general, and especially in the subset with preserved ejection fraction (HFpEF), which is the predominant phenotype in older adults.[6] The objective of this study was to examine the association of a prior heart failure hospitalization with outcomes separately in propensity score-matched cohorts of hospitalized older patients with HFpEF and HFrEF.

Methods

Data Source and Study Patients

We used data from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF), a national hospital-based registry designed to improve the standard of heart failure care and increase adherence to guideline directed medical therapy.[7,8] The OPTIMIZE-HF registry is comprised of 48,612 heart failure hospitalizations in 259 hospitals in 48 states between March 1, 2003, and December 31, 2004. It includes data on demographics, characteristics of patients, quality of care, and outcomes, which were accessed using an internet-based information system.

Assembly of Study Cohorts

Of 48,612 heart failure hospitalizations in the OPTIMIZE-HF registry, 26,376 were Medicare-linked and 25,345 of these patients were discharged alive from the hospital. We excluded 2854 patients with a new diagnosis of heart failure as these patients could not be categorized as having a prior heart failure hospitalization. Of the 22,491 patients with known heart failure, 7648 had HFpEF (ejection fraction ≥50%), of whom 927 had a prior heart failure hospitalization within six months of index hospitalization which was ascertained from Medicare data (Figure 1). Of the remaining 6721 patients who did not have a heart failure hospitalization in the six months prior to the index hospitalization, 1094 (16%) had a heart failure hospitalization longer than six months prior. Using a multivariable logistic regression model, we estimated propensity scores for prior heart failure hospitalization within six months of the index heart failure hospitalization for each of the 7648 patients with HFpEF using 58 baseline characteristics as covariates.[9–11] Using a matching algorithm described elsewhere,[12] we matched 924 of the 927 patients with HFpEF who had a prior heart failure hospitalization with another 924 who did not, thus assembling a matched cohort of 1848 patients with HFpEF (Figure 1), balanced on 58 baseline characteristics (Figure 2). We then repeated the above process in 9558 patients with HFrEF (ejection fraction ≤40%), of whom 1862 had a prior heart failure hospitalization, and assembled a matched cohort of 1844 pairs of patients (Figure 1). Patients with ejection fraction from 41% to 49% (n=5285) were not analyzed.

Outcomes Data

The primary outcome studied was time to all-cause mortality during six (median, two) years of follow-up. Secondary outcomes included times to all-cause and heart failure readmissions. All outcome data, including events and time to events, were collected from the Medicare 100% MedPAR File and the 100% Beneficiary Summary File between January 1, 2002 and December 31, 2008.[13]

Statistical Analysis

We compared between-group baseline characteristics using the Pearson chi-square and Wilcoxon rank sum tests, as appropriate. All outcome analyses were conducted on propensity score-matched data. All-cause mortality associated with prior heart failure hospitalization in HFpEF and HFrEF is displayed as Kaplan-Meier plots (Figure 3). Hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of mortality and readmission associated with prior heart failure hospitalization were estimated using Cox regression models, separately in HFpEF and HFrEF. Time to mortality was defined as the number of days to death for patients who died and number of days to study end as censoring time for those patients who did not die. Time to readmission was defined as the number of days to readmission for patients who had a subsequent readmission. For patients without readmission, censoring time was defined as the number of days to death or study end, whichever occurred first.

We conducted formal sensitivity analyses using Rosenbaum's approach to determine if significant associations observed in our matched data could be explained by an unmeasured covariate.[14] From the 924 pairs of matched patients, we identified pairs in which we could determine which member of the pair clearly had a longer survival or event-free survival time. For example, if one member of a pair died at six months and other member was censored at 12 months, then clearly the second member outlived the other member. In contrast, if one member of a pair is censored at six months and other member died at 12 months, then one could not definitively determine which member of the pair has survived longer. We then tested whether, in the absence of a hidden bias, if patients in the prior heart failure hospitalization group had shorter survival times than their matched counterparts. A significant sign-score test would provide strong evidence of a relationship between prior heart failure hospitalization and time to a particular event. The sign-score test was used to calculate "sensitivity bounds" for a hypothetical unmeasured confounder to determine how much it would need to increase the odds of prior heart failure hospitalization to explain away the significant associations of prior heart failure hospitalization with outcomes. Our sensitivity analysis assumed that the potential unmeasured confounder was a binary baseline characteristic that was a near perfect predictor of the outcomes, which was also not strongly correlated with any of 58 baseline characteristics used in our propensity score model. However, sensitivity analysis cannot determine if such an unmeasured confounder exists. All statistical tests were 2-tailed, and a p value <0.05 was considered significant. All statistical analyses were conducted using IBM SPSS Statistics for Windows software, version 24 (IBM, Armonk, New York).

Results

The 1848 matched patients with HFpEF had a mean age of 78 (±11) years; 90% were ≥65 years, 69% were women, and 15% were African American. Before matching, patients with a prior heart failure hospitalization generally had higher comorbidity and symptom burdens, and a greater proportion was receiving diuretics and digoxin, which were balanced after matching (Table 1a). Absolute standardized differences for all 58 baseline characteristics were <10% in the matched data, suggesting no residual between-group imbalances of confounding consequence (Figure 2).[15] Pre-match and post-match baseline characteristics of patients with HFrEF are displayed in Table 1b.

Mortality in the Matched HFpEF Cohort

All-cause mortality occurred in 81% and 71% of patients with and without a prior heart failure hospitalization, respectively during six (median, two) years of follow-up (HR associated with time to a prior heart failure hospitalization, 1.35; 95% CI, 1.21–1.50; p<0.001; Table 2, Figure 3). In 93% (861/924) of the matched pairs, we were able to determine which member of the pair had a shorter time to death, and in 59% (510/861) of those pairs, patients with a shorter survival time belonged to the group with prior heart failure hospitalization (sign-score test p <0.0001). A hidden covariate that is a near-perfect predictor of mortality would need to increase the odds of prior heart failure hospitalization by 21% before it could explain away this association. There was no heterogeneity in the association between prior heart failure hospitalization and all-cause mortality among various clinically relevant subgroups (Figure 4). HRs (95% CIs) for 30-day and 1-year all-cause mortality were 1.65 (1.15–2.39; p=0.007) and 1.44 (1.23–1.68; p<0.001), respectively (Table 2).

Readmissions in the Matched HFpEF Cohort

All-cause readmission occurred in 90% of patients in both groups (HR associated with time to prior heart failure hospitalization, 1.34; 95% CI, 1.21–1.47; p<0.001; Table 2). In 829 of 924 matched pairs, we were able to determine which member of the pair had a shorter time to all-cause readmission, and in 60% (495/829) of those pairs, those with a shorter readmission-free survival belonged to the group with prior heart failure hospitalization (sign-score test p <0.001). A hidden covariate that is a near-perfect predictor of all-cause readmission would need to increase the odds of prior heart failure hospitalization by 22% before it could explain away this association.

Heart failure readmission occurred in 60% and 44% of patients with and without a prior heart failure hospitalization, respectively (HR, 1.90; 95% CI, 1.67–2.16; p<0.001; Table 2).

Of the 861 matched pairs with time to heart failure readmission data for both members of the pair, this time was shorter in 68% (393/861) of those in the prior heart failure hospitalization group (sign-score test p <0.001). A hidden covariate that is a near-perfect predictor of heart failure readmission would need to increase the odds of prior heart failure hospitalization by 44% before it could explain away this association.

Mortality in the Matched HFrEF Cohort

All-cause mortality occurred in 79% and 73% of patients with and without prior heart failure hospitalization, respectively (HR 1.17; 95% CI 1.09–1.26; p<0.001; Table 3, Figure 3). In 1728 out of 1844 matched pairs, we were able to determine which patient within a pair had a shorter time to death, and 55% (951/1728) of those pairs belonged to the group with a prior heart failure hospitalization (sign-score test p <0.001). A hidden covariate that is a near-perfect predictor of mortality would need to increase the odds of prior heart failure hospitalization by 10% before it could explain away this association.

Readmissions in the Matched HFrEF Cohort

HRs (95% CIs) for all-cause readmission and heart failure readmission associated with a prior heart failure hospitalization were 1.32 (1.23–1.41; p<0.001) and 1.48 (1.37–1.61; p<0.001; Table 3). Of the 1844 matched pairs, we were able to determine time to all-cause and heart failure readmission in 1615 and 1268 pairs of patients, respectively, and in 58% (935/1615) and 62% (785/1268) of those pairs, patients in the prior heart failure hospitalization group had shorter readmission-free survival (sign-score test p for both <0.001). A hidden covariate would need increase the odds of prior heart failure hospitalization by 20% and 31%, respectively, to explain away these associations.

Discussion

Findings from our study demonstrate that a prior heart failure hospitalization is associated with higher risks for short- and long-term all-cause mortality, all-cause readmission and heart failure readmission in patients with HFpEF. We also observed similar associations in patients with HFrEF. Interestingly, the relative risks for all-cause mortality and heart failure readmission appeared to be higher in HFpEF than in HFrEF. To the best of our knowledge, this is the first study to report adverse outcomes associated with a prior heart failure hospitalization in propensity score-matched cohorts of hospitalized older patients with HFpEF and HFrEF. These results suggest that a prior heart failure hospitalization is prognostically as, or perhaps even more significant in HFpEF than in HFrEF.

There are several potential explanations for the findings of our study. Patients with a prior heart failure hospitalization likely represent those with more advanced disease and a higher burden of comorbidities. Before matching, more patients with a prior heart failure hospitalization had dyspnea at rest, jugular venous pressure elevation, and received digoxin and loop diuretics, which are all markers of worse outcomes.[16–18] These patients also had a higher burden of comorbidities such as coronary artery disease, diabetes mellitus, atrial fibrillation, chronic obstructive pulmonary disease and anemia. Although between-group distribution of these and other characteristics were balanced in our matched cohort, matching may not balance for their severity. For example, 48% of patients in our matched cohort had diabetes, but it is possible that those in the prior heart failure hospitalization group had more severe or advanced diabetes. Furthermore, if the reasons for the higher prevalence of diabetes or use of diuretics persisted during follow-up, then they would be expected to become imbalanced and have poor outcomes.

Hospitalization due to acute decompensation of heart failure is often associated with a relatively heightened and more sustained neurohormonal activation, which may further contribute to the poor outcomes in the group with a prior heart failure hospitalization.[5,19,20] Furthermore, more aggressive therapeutic strategies with the use of intravenous loop diuretics and inotropes can lead to further neurohormonal activation, electrolyte imbalance and worsening kidney function, thus increasing the risk of poor outcomes among patients with prior heart failure hospitalization.[18,21–23] Finally, non-adherence to prescribed diet and therapy is known to contribute to heart failure hospitalizations.[24] If patients with a prior heart failure hospitalization continue to be less adherent to their diet and drugs, that would be expected to contribute to poor outcomes.

An interesting observation of our study is that prior heart failure hospitalization-associated risks of all-cause mortality and heart failure readmission were higher in patients with HFpEF than in those with HFrEF. A potential explanation is that adverse effects are often less pronounced in subsets of patients that have higher baseline risk or event rates. For example, the absolute risk of 30-day heart failure readmission was 8% higher in both HFrEF (20% – 12% = 8%) and HFpEF (15% – 7% = 8%). However, because of the higher baseline risk in HFrEF (12%) than in HFpEF (7%), the relative risk was lower in HFrEF. In contrast, baseline risks of 30-day all-cause readmission were similar (25% and 24%) for HFrEF and HFpEF, and relative risks were also similar: 44% and 48% for HFrEF and HFpEF, respectively. Furthermore, competing risk factors for poor outcomes in HFrEF might be stronger than in HFpEF. For example, fatal ventricular arrhythmias are more common in HFrEF than in HFpEF and a higher incidence of sudden cardiac death in patients with HFrEF would attenuate the risk of death associated with a prior heart failure hospitalization.[25,26]

Several previous studies have examined the association of prior heart failure hospitalization with outcomes in patients with chronic heart failure.[1–5] A prior heart failure hospitalization is associated with higher risks of subsequent poor outcomes among ambulatory patients with HFrEF or HFpEF.[1,2] The current study is distinguished by its large sample size, national representation, use of propensity scores to assemble balanced cohorts, sensitivity analyses, subgroup analyses, and comparison with HFrEF. Our study findings have important clinical implications. The HFpEF phenotype is characteristically, prognostically and therapeutically different form HFrEF. Findings from our study suggest that a heart failure hospitalization in the past six months can be used to risk stratify patients with HFpEF who might be at a higher risk for worse outcomes.

There are several limitations of this study. Despite our use of propensity score-matching, confounding resulting from residual bias or to unmeasured covariates is possible. However, findings from post-match absolute standardized differences suggest that residual biases of

58 variables used in the propensity score model were inconsequential and findings from the sensitivity analyses suggest that these results were relatively immune to bias by unmeasured confounders. Patients in the prior heart failure hospitalization group had to survive up to six months to have a heart failure readmission during index hospitalization. However, this survivor cohort phenomenon may have attenuated the true association between a prior heart failure hospitalization and subsequent outcomes. Our study is based on fee-for-service Medicare beneficiaries, which may limit generalizability.

Conclusions

Among hospitalized older patients with HFpEF, a heart failure hospitalization in the past six months is associated with higher risks of all-cause mortality, all-cause readmission and heart failure readmission, with relative risks which were similar to or perhaps greater than those observed in HFrEF. Future studies need to replicate these findings in more contemporary patient populations, and to develop and test interventions that may improve outcomes in patients with HFpEF and a prior heart failure hospitalization.

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Clinical Significance

- Among hospitalized older patients with heart failure with preserved ejection fraction (HFpEF), a heart failure hospitalization within prior six months is associated with higher risks of mortality and readmissions.
- These risks are similar to those observed in patients with heart failure with reduced ejection fraction (HFrEF).
- The relative risks of mortality and heart failure readmission appear to be higher in HFpEF than in HFrEF.

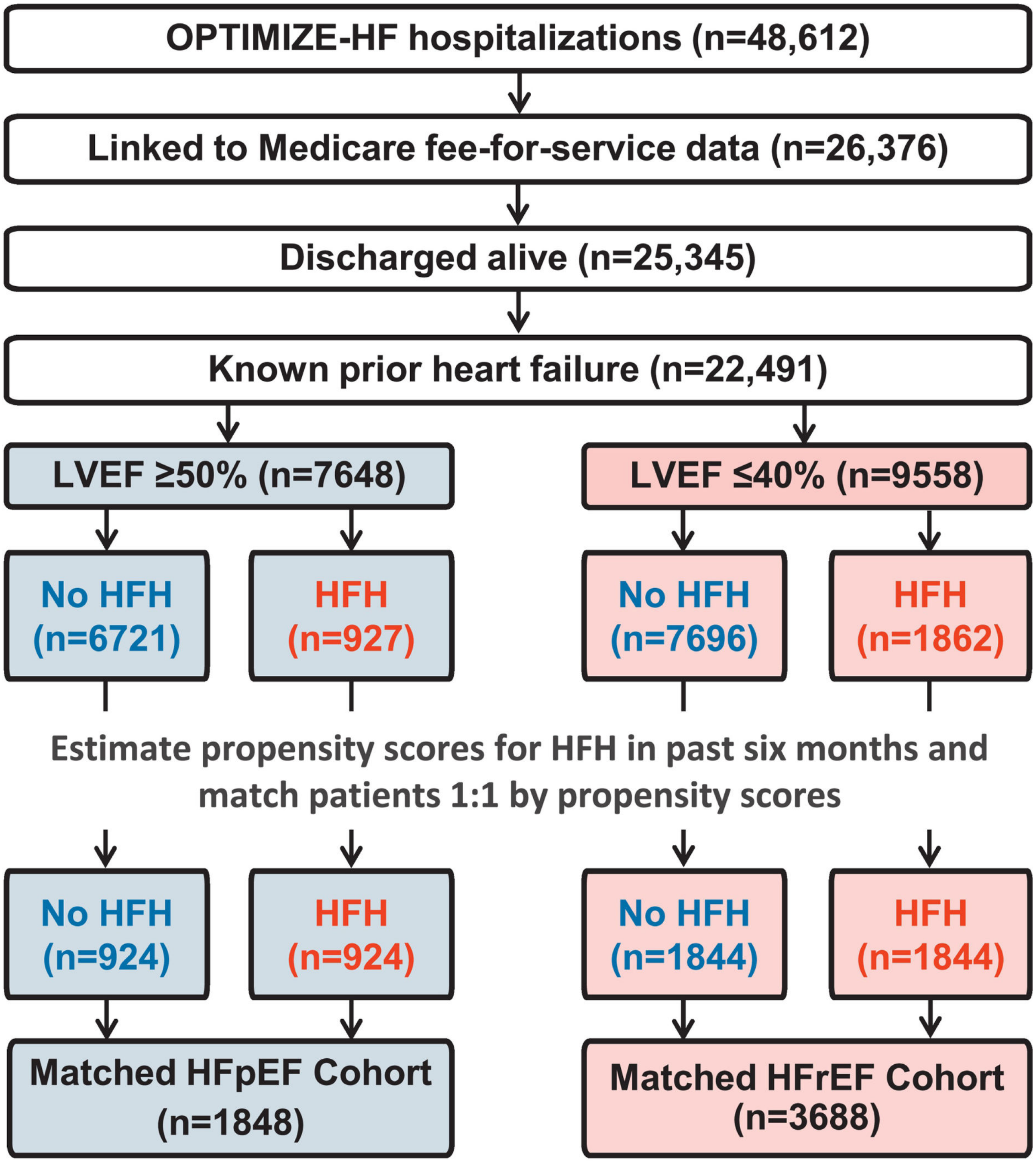

Figure 1.
Flow chart displaying assembly of propensity score-matched cohorts of patients by a heart failure hospitalization (HFH) in the six months prior to the index HFH (HFH = Heart failure hospitalization; HFpEF = Heart failure with preserved ejection fraction; HFrEF = Heart failure with reduced ejection fraction; LVEF = Left ventricular ejection fraction; OPTIMIZE-HF = Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure)

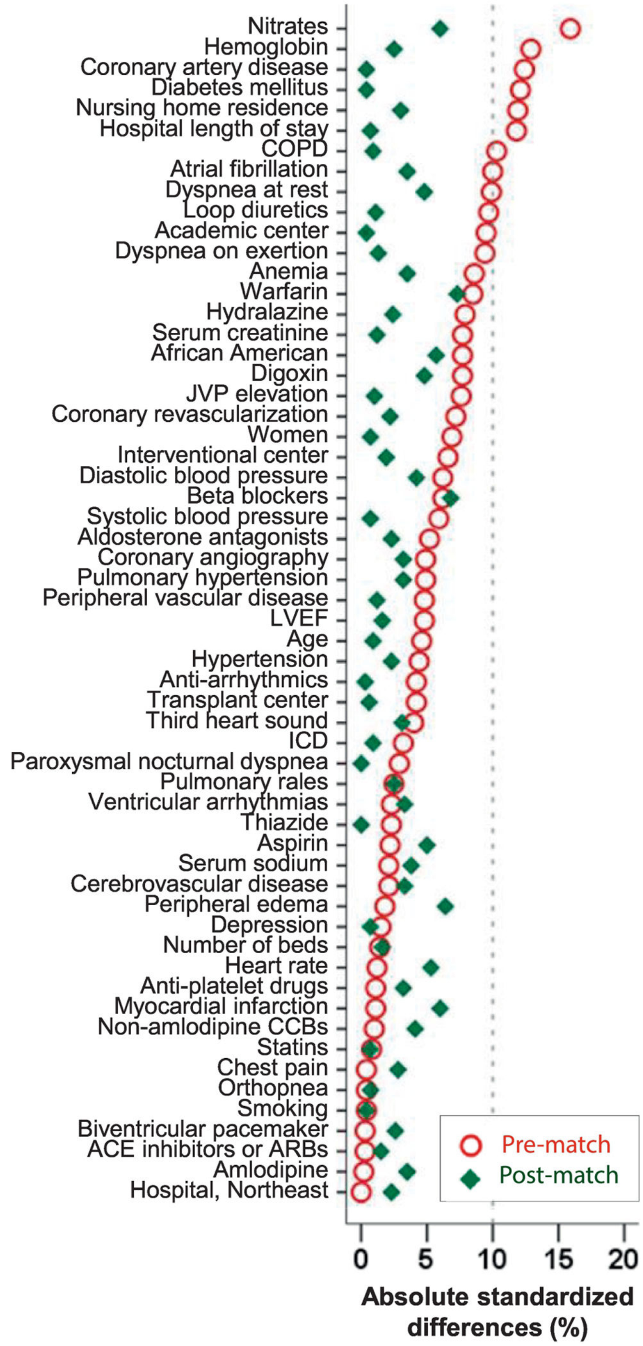

Figure 2.

Love plot displaying absolute standardized differences comparing 58 baseline characteristics of 7648 pre-match and 1848 matched patients with heart failure with preserved ejection fraction, by prior versus no prior heart failure hospitalization in past six months, before and after propensity score matching. An absolute standardized difference of 0% indicates no residual bias and values <10% indicate inconsequential bias (ACE = Angiotensin-converting enzyme; ARB = Angiotensin receptor blockers; CCBs = Calcium channel blockers; COPD =

Chronic obstructive pulmonary disease; ICD =Implantable cardioverter-defibrillator; JVP = Jugular venous pressure; LVEF = Left ventricular ejection fraction)

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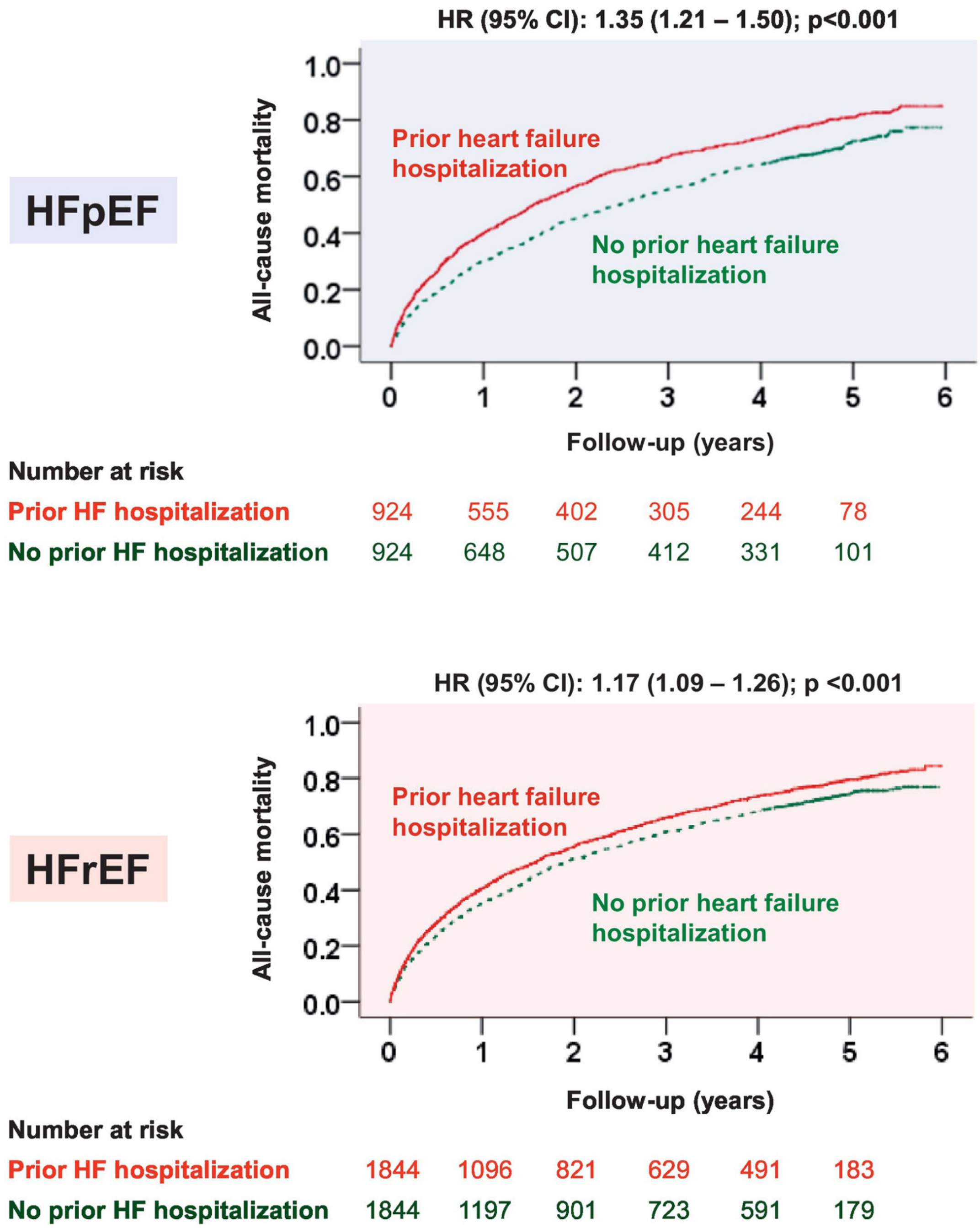

Figure 3.

Kaplan-Meier plots for all-cause mortality during six years of post-discharge follow up by heart failure hospitalization during six months prior to the index hospitalization in 924 and 1844 pairs of propensity score-matched patients with heart failure with preserved ejection fraction (HFpEF; top panel) and heart failure with reduced ejection fraction (HFrEF; bottom panel), respectively (CI = Confidence interval; HR = Hazard ratio).

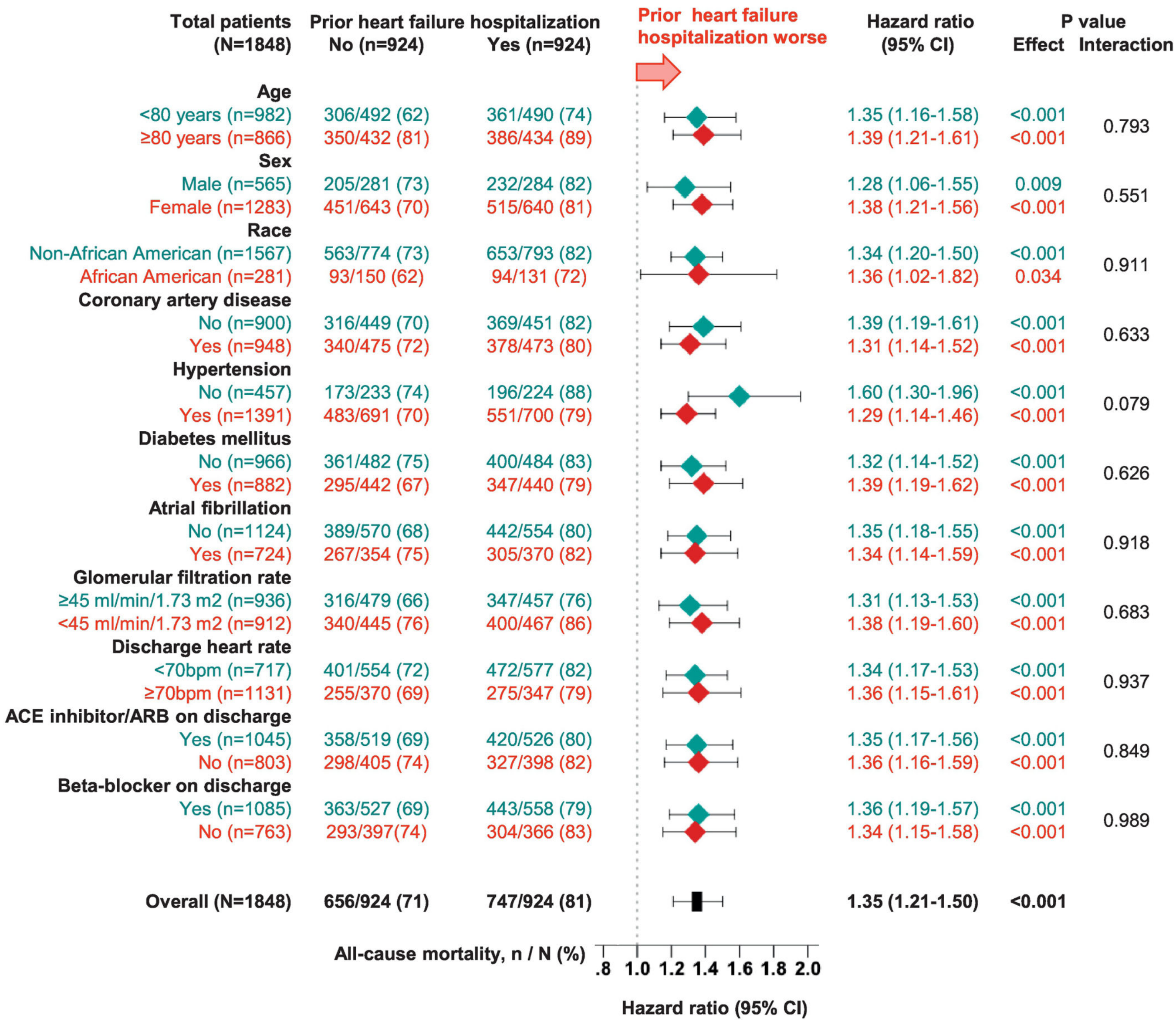

Figure 4.

Forest plots displaying associations of heart failure hospitalization in the six months prior to index hospitalization and all-cause mortality during six years of follow-up in clinically relevant subgroups of propensity score-matched patients with heart failure with preserved ejection fraction (≥50%) (ACE = Angiotensin-converting enzyme; ARB = Angiotensin receptor blocker; CI = Confidence interval)

Table 1a.

Baseline Characteristics of Hospitalized Older Patients with Heart Failure with Preserved Ejection Fraction (≥50%), by Hospitalization due to Heart Failure in the Past Six Months

Mean (±standard deviation) or n (%)	Before propensity score matching (n=7648)			After propensity score matching (n=1848)		
	Heart failure hospitalization in six months prior to the index hospitalization			Heart failure hospitalization in six months prior to the index hospitalization		
	No (n=6721)	Yes (n=927)	P value	No (n=924)	Yes (n=924)	P value
Age (years)	78 (±11)	78 (±11)	0.183	78 (±11)	78 (±11)	0.848
Women	4444 (66%)	643 (69%)	0.050	643 (70%)	640 (69%)	0.880
African American	797 (12%)	134 (14%)	0.023	150 (16%)	131 (14%)	0.218
Left ventricular ejection fraction (%)	57 (±6)	56 (±6)	0.180	57 (±6)	56 (±6)	0.726
Smoker in past 1 year	645 (10%)	90 (10%)	0.914	91 (10%)	90 (10%)	0.938
Admission from nursing home	122 (2%)	35 (4%)	<0.001	28 (3%)	33 (4%)	0.515
Past medical history						
Hypertension	5214 (78%)	702 (76%)	0.207	691 (75%)	700 (76%)	0.627
Coronary artery disease	3037 (45%)	476 (51%)	<0.001	475 (51%)	473 (51%)	0.926
Diabetes mellitus	2801 (42%)	442 (48%)	0.001	442 (48%)	440 (48%)	0.926
Cerebrovascular disease	1200 (18%)	173 (19%)	0.548	184 (20%)	172 (19%)	0.479
Peripheral vascular disease	971 (14%)	150 (16%)	0.162	151 (16%)	147 (16%)	0.800
Atrial fibrillation	2378 (35%)	373 (40%)	0.004	354 (38%)	370 (40%)	0.446
Chronic obstructive pulmonary disease	2054 (31%)	328 (35%)	0.003	330 (36%)	326 (35%)	0.846
Anemia	1458 (22%)	235 (25%)	0.012	220 (24%)	234 (25%)	0.449
Depression	853 (13%)	113 (12%)	0.666	110 (12%)	112 (12%)	0.886
Admission findings						
Dyspnea on exertion	4239 (63%)	542 (58%)	0.007	548 (59%)	542 (59%)	0.777
Dyspnea at rest	2874 (43%)	442 (48%)	0.005	418 (45%)	440 (48%)	0.305
Orthopnea	1686 (25%)	231 (25%)	0.913	234 (25%)	231 (25%)	0.872
Paroxysmal nocturnal dyspnea	891 (13%)	114 (12%)	0.418	114 (12%)	114 (12%)	1.000
Chest pain	1506 (22%)	206 (22%)	0.899	215 (23%)	204 (22%)	0.541
Jugular venous pressure elevation	1661 (25%)	260 (28%)	0.028	253 (27%)	257 (28%)	0.835
Third heart sound	384 (6%)	62 (7%)	0.235	54 (6%)	61 (7%)	0.500
Pulmonary rales	4299 (64%)	604 (65%)	0.478	591 (64%)	602 (65%)	0.593
Peripheral edema	4452 (66%)	622 (67%)	0.604	593 (64%)	621 (67%)	0.170
Serum sodium (mEq/L)	137 (±10)	137 (±11)	0.540	136 (±13)	137 (±11)	0.408
Hemoglobin (g/dL)	11.8 (±2.8)	11.4 (±3.5)	<0.001	11.5 (±3.4)	11.4 (±3.5)	0.594
Discharge findings						
Heart rate (bpm)	74 (±14)	74 (±14)	0.736	73 (±14)	74 (±14)	0.254

Mean (±standard deviation) or n (%)	Before propensity score matching (n=7648)			After propensity score matching (n=1848)		
	Heart failure hospitalization in six months prior to the index hospitalization			Heart failure hospitalization in six months prior to the index hospitalization		
	No (n=6721)	Yes (n=927)	P value	No (n=924)	Yes (n=924)	P value
Systolic blood pressure (mmHg)	130 (±22)	129 (±22)	0.089	129 (±22)	129 (±22)	0.874
Diastolic blood pressure (mmHg)	66 (±12)	65 (±12)	0.076	65 (±12)	65 (±12)	0.370
Serum creatinine (mg/dL)	1.7 (±1.4)	1.8 (±1. 4)	0.025	1.8 (±1.6)	1.8 (±1. 4)	0.789
Discharge medications						
ACE inhibitors or ARBs	3811 (57%)	527 (57%)	0.932	519 (56%)	526 (57%)	0.743
Beta blockers	3864 (57%)	561 (61%)	0.080	527 (57%)	558 (60%)	0.143
Aldosterone antagonists	512 (8%)	84 (9%)	0.124	78 (8%)	84 (9%)	0.622
Digoxin	1237 (18%)	199 (21%)	0.025	180 (19%)	198 (21%)	0.299
Loop diuretics	5049 (75%)	734 (79%)	0.007	728 (79%)	732 (79%)	0.819
Nitrates	1627 (24%)	290 (31%)	<0.001	314 (34%)	288 (31%)	0.197
Amlodipine	781 (12%)	107 (12%)	0.945	96 (10%)	106 (11%)	0.456
Other calcium channel blockers	1236 (18%)	167 (18%)	0.782	182 (20%)	167 (18%)	0.373
Hospital length of stay (days)	5.7 (±4.8)	6.3 (±5.1)	0.001	6.3 (±6.0)	6.3 (±5.1)	0.874
Hospital characteristics						
Beds (numbers)	395 (±247)	398 (±221)	0.708	395 (±241)	398 (±221)	0.737
Academic center	2830 (42%)	434 (47%)	0.007	434 (47%)	432 (47%)	0.926
Interventional center	5152 (77%)	736 (79%)	0.063	740 (80%)	733 (79%)	0.686
Heart transplant center	971 (14%)	148 (16%)	0.220	149 (16%)	147 (16%)	0.899

ACE= Angiotensin-converting enzyme; ARBs = Angiotensin receptor blockers

Table 1b.

Baseline Characteristics of Hospitalized Older Patients with Heart Failure with Reduced Ejection Fraction (≤40%), by Hospitalization due to Heart Failure in Prior Six Months

Mean (±standard deviation) or n (%)	Before propensity score matching (n=9558)			After propensity score matching (n=3688)		
	Heart failure hospitalization in six months prior to the index hospitalization			Heart failure hospitalization in six months prior to the index hospitalization		
	No (n=7696)	Yes (n=1862)	P value	No (n=1844)	Yes (n=1844)	P value
Age (years)	76 (±10)	74 (±12)	<0.001	74 (±11)	74 (±12)	0.759
Women	3135 (41%)	800 (43%)	0.079	812 (44%)	793 (43%)	0.528
African American	993 (13%)	400 (22%)	<0.001	405 (22%)	389 (21%)	0.522
Left ventricular ejection fraction (%)	27 (±8)	25 (±9)	<0.001	25 (±8)	25 (±8)	0.705
Smoker in past 1 year	1011 (13%)	265 (14%)	0.212	263 (14%)	261 (14%)	0.925
Admission from nursing home	97 (1%)	40 (2%)	0.004	34 (2%)	38 (2%)	0.634
Past medical history						
Hypertension	5186 (67%)	1229 (66%)	0.255	1223 (66%)	1218 (66%)	0.862
Coronary artery disease	4644 (60%)	1179 (63%)	0.018	1150 (62%)	1169 (63%)	0.517
Diabetes mellitus	3083 (40%)	871 (47%)	<0.001	863 (47%)	861 (47%)	0.947
Cerebrovascular disease	1248 (16%)	281 (15%)	0.235	277 (15%)	278 (15%)	0.963
Peripheral vascular disease	1248 (16%)	298 (16%)	0.824	306 (17%)	296 (16%)	0.656
Atrial fibrillation	2603 (34%)	664 (36%)	0.134	656 (36%)	657 (36%)	0.973
Chronic obstructive pulmonary disease	2073 (27%)	554 (30%)	0.015	536 (29%)	548 (30%)	0.664
Anemia	1231 (16%)	323 (17%)	0.156	319 (17%)	321 (17%)	0.931
Depression	757 (10%)	187 (10%)	0.789	187 (10%)	186 (10%)	0.956
Admission findings						
Dyspnea on exertion	4941 (64%)	1123 (60%)	0.002	1108 (60%)	1120 (61%)	0.686
Dyspnea at rest	3279 (43%)	870 (47%)	0.001	855 (46%)	855 (46%)	1.000
Orthopnea	2093 (27%)	556 (30%)	0.021	544 (30%)	546 (30%)	0.942
Paroxysmal nocturnal dyspnea	1245 (16%)	312 (17%)	0.544	302 (16%)	308 (17%)	0.790
Chest pain	1643 (21%)	382 (21%)	0.430	371 (20%)	380 (21%)	0.713
Jugular venous pressure elevation	2398 (31%)	688 (37%)	<0.001	699 (38%)	678 (37%)	0.475
Third heart sound	872 (11%)	259 (14%)	0.002	279 (15%)	253 (14%)	0.223
Pulmonary rales	4850 (63%)	1184 (64%)	0.649	1183 (64%)	1172 (64%)	0.706
Peripheral edema	4674 (61%)	1210 (65%)	0.001	1190 (65%)	1195 (65%)	0.863
Serum sodium (mEq/L)	137 (±10)	136 (±12)	0.007	136 (±12)	136 (±12)	0.965
Hemoglobin (g/dL)	12.4 (±2.3)	12.1 (±3.8)	<0.001	12.2 (±2.8)	12.1 (±3.8)	0.579
Discharge findings						
Heart rate (bpm)	75 (±13)	76 (±13)	0.018	76 (±13)	76 (±13)	0.743

Mean (±standard deviation) or n (%)	Before propensity score matching (n=9558)			After propensity score matching (n=3688)		
	Heart failure hospitalization in six months prior to the index hospitalization			Heart failure hospitalization in six months prior to the index hospitalization		
	No (n=7696)	Yes (n=1862)	P value	No (n=1844)	Yes (n=1844)	P value
Systolic blood pressure (mmHg)	121 (±21)	118 (±20)	<0.001	118 (±20)	118 (±20)	0.974
Diastolic blood pressure (mmHg)	66 (±12)	65 (±12)	0.005	65 (±12)	65 (±12)	0.541
Serum creatinine (mg/dL)	1.7 (±1.2)	1.9 (±1.4)	<0.001	1.9 (±1.3)	1.9 (±1.4)	0.853
Discharge medications						
ACE inhibitors or ARBs	5294 (69%)	1240 (67%)	0.068	1235 (67%)	1227 (67%)	0.780
Beta blockers	5505 (72%)	1323 (71%)	0.682	1310 (71%)	1312 (71%)	0.942
Aldosterone antagonists	1235 (16%)	340 (18%)	0.021	361 (20%)	336 (18%)	0.293
Digoxin	2886 (38%)	800 (43%)	<0.001	756 (41%)	788 (43%)	0.285
Loop diuretics	6120 (80%)	1502 (81%)	0.270	1471 (80%)	1486 (81%)	0.536
Nitrates	2067 (27%)	558 (30%)	0.007	568 (31%)	549 (30%)	0.496
Amlodipine	417 (5%)	90 (5%)	0.312	93 (5%)	90 (5%)	0.820
Other calcium channel blockers	527 (7%)	103 (6%)	0.040	105 (6%)	103 (6%)	0.886
Hospital length of stay (days)*	5.9 (5.5)	6.5 (9.7)	<0.001	6.1 (6.0)	6.5 (9.7)	0.234
Hospital characteristics*						
Number of beds	426 (255)	442 (251)	0.015	442 (252)	441 (250)	0.918
Academic center	3634 (47%)	1005 (54%)	<0.001	1015 (55%)	993 (54%)	0.467
Interventional center	6070 (79%)	1527 (82%)	0.003	1533 (83%)	1509 (82%)	0.298
Heart transplant center	1273 (17%)	399 (21%)	<0.001	376 (20%)	391 (21%)	0.543

ACE = Angiotensin-converting enzyme; ARB = Angiotensin receptor blocker

Table 2.

Outcomes in 1848 Propensity Score-Matched Hospitalized Older Patients with Heart Failure with Preserved Ejection Fraction (≥50%), by Hospitalization due to Heart Failure in the Past Six Months

	Events (%) by heart failure hospitalization in six months prior to the index hospitalization		Hazard ratio associated with prior hospitalization due to heart failure (95% CIs); p value
	No (n=924)	Yes (n=924)	
30-day outcomes			
All-cause mortality	46 (5%)	75 (8%)	1.65 (1.15–2.39); p=0.007
All-cause readmission	221 (24%)	308 (33%)	1.48 (1.24–1.75); p<0.001
Heart failure readmission	65 (7%)	137 (15%)	2.21 (1.65–2.97); p<0.001
1-year outcomes			
All-cause mortality	276 (30%)	369 (40%)	1.44 (1.23–1.68); p<0.001
All-cause readmission	656 (71%)	723 (78%)	1.37 (1.23–1.52); p<0.001
Heart failure readmission	266 (29%)	423 (46%)	1.99 (1.70–2.32); p<0.001
Overall outcomes			
All-cause mortality	656 (71%)	747 (81%)	1.35 (1.21–1.50); p<0.001
All-cause readmission	827 (90%)	830 (90%)	1.34 (1.21–1.47); p<0.001
Heart failure readmission	407 (44%)	552 (60%)	1.90 (1.67–2.16); p<0.001

Table 3.

Outcomes in 3688 Propensity Score-Matched Hospitalized Older Patients with Heart Failure with Reduced Ejection Fraction (≤40%), by Hospitalization due to Heart Failure in the Past Six Months

	Events (%) by heart failure hospitalization in six months prior to the index hospitalization		Hazard ratio associated with prior hospitalization due to heart failure (95% CIs); p value
	No (n=1844)	Yes (n=1844)	
30-day outcomes			
All-cause mortality	131 (7%)	158 (9%)	1.22 (0.96 –1.53); p=0.099
All-cause readmission	462 (25%)	623 (34%)	1.44 (1.28–1.63); p<0.001
Heart failure readmission	225 (12%)	365 (20%)	1.72 (1.46–2.03); p<0.001
1-year outcomes			
All-cause mortality	647 (35%)	748 (41%)	1.21 (1.09 –1.34); p=0.001
All-cause readmission	1273 (69%)	1455 (79%)	1.40 (1.30 –1.51); p<0.001
Heart failure readmission	763 (41%)	1007 (55%)	1.56 (1.42 –1.72); p<0.001
Overall outcomes			
All-cause mortality	1354 (73%)	1463 (79%)	1.17 (1.09 –1.26); p<0.001
All-cause readmission	1595 (86%)	1637 (89%)	1.32 (1.23 –1.41); p<0.001
Heart failure readmission	1061 (58%)	1249 (68%)	1.48 (1.37 –1.61); p<0.001