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Systolic Blood Pressure and Outcomes in Older Patients with HFpEF and Hypertension

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Abstract

Background—New hypertension and heart failure guidelines recommend that systolic blood pressure (SBP) in patients with heart failure with preserved ejection fraction (HFpEF) and hypertension be lowered to <130 mmHg.

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Methods—Of the 6778 hospitalized patients with HFpEF and a history of hypertension in the Medicare-linked OPTIMIZE-HF registry, 3111 had a discharge SBP <130 mmHg. Using propensity scores for SBP <130 mmHg, we assembled a matched cohort of 1979 pairs with SBP <130 versus ≥130 mmHg, balanced on 66 baseline characteristics (mean age, 79 years; 69% women; 12% African American). We then assembled a second matched cohort of 1326 pairs with SBP <120 versus ≥130 mmHg. Hazard ratios (HRs) and 95% confidence intervals (CIs) for outcomes associated with SBP <130 and <120 mmHg were separately estimated in the matched cohort using SBP ≥130 mmHg as the reference.

Results—HRs (95% CIs) for 30-day, 12-month, and 6-year all-cause mortality associated with SBP <130 mmHg were 1.20 (0.91–1.59; p=0.200), 1.11 (0.99–1.26; p=0.080), and 1.05 (0.98–1.14; p=0.186), respectively. Respective HRs (95% CIs) associated with SBP <120 mmHg were 1.68 (1.21–2.34; p=0.002), 1.28 (1.11–1.48; p=0.001), and 1.11 (1.02–1.22; p=0.022). There was no association with readmission.

Conclusions—Among older patients with HFpEF and hypertension, compared with SBP ≥130 mmHg, the new target SBP <130 mmHg had no association with outcomes, but SBP <120 mmHg was associated with a higher risk of death but not of readmission. Future prospective studies need to evaluate optimal SBP treatment goals in these patients.

Keywords

Systolic blood pressure; heart failure with preserved ejection fraction; all-cause mortality; readmission

According to the 2017 American College of Cardiology Foundation / American Heart Association (ACCF/AHA) high blood pressure guideline, systolic blood pressure (SBP) ≥130 mmHg is considered to be hypertension with SBP <120 mmHg as normal, and values between 120 and 129 mmHg as elevated.[1] The 2017 update of the ACCF/AHA heart failure guideline recommends that SBP in patients with heart failure with preserved ejection fraction (HFpEF) and persistent hypertension should be controlled to an optimal target SBP of <130 mmHg.[2] However, to the best of our knowledge, outcomes of patients with HFpEF and hypertension with a controlled and normal SBP have not been directly compared with a propensity score-matched group of patients with HFpEF and hypertension with an uncontrolled SBP. Therefore, the objective of the current study was to examine the association of SBP <130 mmHg with outcomes compared with SBP ≥130 mmHg in a propensity score-matched cohort of patients with HFpEF and hypertension.

Methods

Data Source and Study Population

The current analyses are based on data from the Medicare-linked OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) registry, the details of which have been presented before.[3–8] The registry included extensive information on 48,612 HF hospitalizations occurring in 259 hospitals in 48 states from 2003–2004. Long-term outcomes data were obtained by linking 26,376 unique OPTIMIZE-HF patients to the Medicare data by probabilistic linking.[4] Of these, 25,354

patients were discharged alive. HFpEF was defined as left ventricular ejection fraction ≥50%. Of the 8,873 patients with HFpEF, 6,842 had a history of hypertension.

Admission and discharge SBP values were obtained with patients in the supine position, and automated electronic data checks were used to prevent outlying SBP values.[9] After excluding 56 patients with missing discharge SBP data and five patients with a discharge SBP <60 mmHg, the sample size consisted of 6,778 patients (Figure 1). These patients had a mean (±SD) discharge SBP of 132 (±22) mmHg (median, 131, minimum 60, maximum 232, interquartile range, 30 mmHg). Of the 6,778 patients with HFpEF and hypertension, 3,678 (54%) had SBP ≥130 mmHg and 3,100 (46%) had SBP <130 mmHg. Of the 3,100 patients with SBP <130 mmHg, 1,111 (36%) had SBP 120–129 mmHg and 1,989 (64%) had SBP <120 mmHg.

Assembly of a Balanced Cohort

Our preliminary analysis demonstrated that there were significant between-group imbalances in several baseline characteristics, including several potential confounders (Table 1). To minimize the effect of confounding between SBP and outcomes, we used propensity scores to assemble a matched cohort in which patients would be balanced on all key measured baseline characteristics.[10, 11] We used a non-parsimonious multivariable logistic regression model to estimate propensity scores for having a discharge SBP <130 mmHg for each of the 6778 patients.[12–15] The 66 baseline characteristics displayed in Figure 2 were used as covariates in the model. Using a greedy matching protocol, we then matched 1979 (64% of 3100) patients with SBP <130 with another 1979 patients who had a discharge SBP ≥130 mmHg but had the propensity score for having SBP <130 mmHg.[16–18] We then estimated absolute standardized differences for each of the 66 baseline characteristics in both pre-match and matched cohorts. An absolute standardized difference for a baseline characteristic is a measure of between-group balance for that variable. Our goal was to achieve absolute standardized difference values for all key measured baseline characteristics to be <10%. Values <10% indicate inconsequential residual bias, and a value of 0% indicates no residual bias.

Assembly of Sensitivity Cohorts

To examine the associations of normal (versus hypertensive) SBP with outcomes, we examined the associations of SBP <120 mmHg using SBP ≥130 mmHg as the reference. As such, we repeated the above process to assemble a propensity score-matched cohort with SBP <120 versus ≥130 mmHg. Of the 1989 patients who had a discharge SBP <120 mmHg, we were able to match 1326 (67%) patients with 1326 who had a discharge SBP ≥130 mmHg but had the propensity score for having SBP <120 mmHg, thus assembling a matched cohort of 2652 patients (Figure 1). Finally, to examine the associations of borderline (versus hypertensive) SBP with outcomes, we examined the associations of SBP 120–129 mmHg using SBP ≥130 mmHg as the reference. Of the 1111 patients with a discharge SBP 120–129 mmHg, we were able to match 1097 (99%) with 1097 patients who had a discharge SBP ≥130 mmHg but had the propensity score for having SBP 120–129 mmHg, thus assembling a matched cohort of 2194 patients (data not shown in Figure 1).

Outcomes Data

Our outcomes included all-cause mortality, all-cause readmission, and HF readmission during 30 days, 12 months, and 6 years of follow-up. All data on outcomes and time to those outcome events were collected from Medicare data.[4]

Statistical Analyses

Pearson's Chi-square and Wilcoxon rank-sum tests were used to compare baseline characteristics between the two SBP groups in the pre-match and matched cohorts. All outcomes analyses comparing outcomes between SBP groups were performed in the matched data. Kaplan-Meier survival analyses were performed to plot all-cause mortality associated with SBP <130 mmHg and <120 mmHg versus ≥130 mmHg. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for outcomes associated with SBP <130 mmHg, <120 mmHg and 120–129 mmHg, each time using SBP ≥130 mmHg as the reference. For each outcome during a given period, patients without that outcome were censored at the end of that period. For example, for 30-day heart failure readmission, patients without a heart failure readmission were censored after 30 days.

Formal sensitivity analyses were conducted to quantify the degree of hidden bias that could potentially explain away any significant associations.[19] To assess the homogeneity of the associations, we examined the associations between SBP <120 mmHg and 2-year all-cause mortality in clinically relevant subgroups of matched patients, including by use of antihypertensive drugs. We used three subgroups of antihypertensive drugs based on the use of renin-angiotensin system inhibitors, beta-blockers, and either of thiazide diuretics, calcium channel blockers, and hydralazine. We chose SBP <120 mmHg and 2-year all-cause mortality for the subgroup analyses to allow adequate power within subgroups. To assess for non-linearity, we fitted restricted cubic spline models with 4 knots at SBPs 120, 130 (reference), 140, and 160 mmHg, using both matched data and the pre-match data adjusting for propensity scores. All statistical analyses were conducted using IBM SPSS Statistics for Windows software, version 24 (IBM Corp., Armonk, NY, USA), and SAS software for Windows, version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Baseline Characteristics

The 3958 matched patients had a mean (±SD) age of 79 (±10) years, an ejection fraction of 57 (±6) %, 69% were women, and 12% were African American. These patients had a mean (±SD) and median (interquartile range) admission SBP of 148 (±32) mmHg and 148 (40) mmHg, respectively (minimum 68 mmHg, maximum 287mmHg). The mean (±SD) and median (interquartile range) discharge SBP were 130 (±19) mmHg and 130 (40) mmHg, respectively (minimum 60 mmHg, maximum 221 mmHg). Only 17 (0.4% of 3958) patients had a discharge SBP of <90 mmHg, and 140 (3.5% of 3958) had a discharge SBP of <100 mmHg. Before matching, patients with a discharge SBP <130 mmHg were older, a higher proportion had diabetes mellitus and atrial fibrillation, and used angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and beta-blockers (Table 1). All 66

baseline characteristics were balanced after matching and had an absolute standardized difference of <10% (Table 1, Figure 2). Baseline characteristics of patients with SBP <120 mm Hg versus ≥130 mm Hg before and after matching are presented in Table 2.

SBP <130 mmHg and All-Cause Mortality

Among the 1979 pairs of matched patients, HRs (95% CIs) for 30-day, 12-month and 6-year all-cause mortality associated with a discharge SBP <130 (versus ≥130) mmHg were 1.20 (0.91–1.59; p=0.200), 1.11 (0.99–1.26; p=0.080) and 1.05 (0.98–1.14; p=0.186), respectively (Table 2, Figure 3). Among the 1097 pairs of matched patients with SBP 120–129 versus ≥130 mmHg, a discharge SBP 120–129 mmHg had no association with mortality (data not shown in tables or figures).

SBP <120 mmHg and All-Cause Mortality

Among the 1326 pairs of matched patients, HRs (95% CIs) for 30-day, 12-month and 6-year all-cause mortality associated with a discharge SBP <120 (versus ≥130) mmHg were 1.68 (1.21–2.34; p=0.002), 1.28 (1.11–1.48; p=0.001) and 1.11 (1.02–1.22; p=0.022), respectively (Table 2, Figure 3). The results of sensitivity analyses are presented as a footnote in Table 3.

Spline Regression Analyses

There was no evidence of a non-linear relationship between SBP and all-cause mortality (p for non-linearity, 0.336; Figure 4). HRs for death associated with SBP started increasing at SBP 170 mmHg, becoming significant at SBP >185 mmHg (only 24 patients had SBP >185 mmHg). The risk of death appears to increase in a linear manner at SBP <130.

Subgroup Analyses

Among the 1326 pairs of matched patients with SBP <120 versus ≥130 mmHg, 2-year all-cause mortality occurred in 45% and 39% of patients with SBP <120 versus ≥130 mmHg, respectively (HR, 1.24; 95% CI, 1.10–1.39; p<0.001; Figure 5). This association was homogenous across clinically relevant subgroups, except that there was a significant 47% higher risk in the smaller subset of 959 patients discharged on antihypertensive drugs and a non-significant 13% higher risk in the larger subset of 1693 patients not discharged on antihypertensive drugs (Figure 5).

Association with Readmissions

Discharge SBP had no association with readmissions at any time period. HRs (95% CIs) for 6-year all-cause readmission associated with SBP <130, 120–129 and <120 mmHg when compared to SBP ≥130 mmHg were 1.03 (0.97–1.10; p=0.334), 0.95 (0.87–1.04; p=0.267) and 1.02 (0.94–1.11; p=0.613), respectively (Table 2). Respective HRs (95% CIs) for 6-year HF readmission were 1.03 (0.94–1.13; p=0.525), 0.92 (0.81–1.05; p=0.219) and 1.00 (0.89–1.12; p=0.992; (Table 2).

Discussion

Findings from the current study demonstrate that older patients with HFpEF and hypertension who were hospitalized for heart failure decompensation and were discharged with SBP controlled at or below the new recommended target of <130 mmHg did not have significantly better outcomes than those discharged with uncontrolled SBP of ≥130 mmHg. In contrast, patients who had a normal discharge SBP of <120 mmHg had a significantly higher risk of death when compared with those with a discharge SBP of ≥130 mmHg. Discharge SBP had no association with readmissions due to heart failure decompensation or other reasons. These findings suggest that unlike in the general population in whom a controlled or normal SBP is associated with improved outcomes, in patients with HFpEF and hypertension, a controlled or normal SBP is not associated with improved outcomes.

The findings from observational studies of SBP in the general population that used similar methodology as in the current study suggest that a lower SBP is associated with improved outcomes.[20, 21] In contrast, in patients with heart failure with reduced ejection fraction (HFrEF), a lower SBP has been shown to be paradoxically associated with worse outcome.[8, 9, 22, 23] This paradoxical association has been attributed to the lower SBP being a dose-dependent marker of impaired left ventricular contractility.[24] Although the underlying mechanism of a similar paradoxical relationship in HFpEF is less clearly understood,[5] it has been suggested that left ventricular contractility is impaired in these patients, which in turn is associated with worse outcomes.[25–28] If a greater degree of drop in SBP is caused by a greater degree of impaired contractility then that would in part also explain the worse outcomes associated with SBP <120 mmHg, but not with SBP 120–129 mmHg. However, impaired contractility is not likely to fully explain the higher risk of death associated with low SBP in HFpEF as there was no associated higher risk of HF readmission. It is possible that a low SBP is also a marker of non-cardiovascular morbidity, which in turn may increase the risk of non-cardiovascular mortality. Patients with HFpEF are more likely to die from non-cardiovascular causes than those with HFrEF.[29] However, a low SBP is also not associated with a higher risk of HF readmission in patients with HFrEF.[8] Thus, it is possible that arrhythmias, also markers of impaired contractility, are more common in patients with low SBP in both HFrEF and HFpEF, which may contribute to sudden deaths that are not associated with a higher risk of hospital readmission. The lower prevalence of pre-match use of antihypertensive drugs in the lower SBP groups in our study (Tables 1 and 2) suggests that they were unlikely to be treatment-related hypotension.

In a prior propensity score-matched cohort of 1802 hospitalized patients with HFpEF, we have demonstrated that a discharge SBP <120 mmHg (versus ≥120 mmHg) was associated with a 24% significantly higher risk of death in the smaller subset of 612 patients without hypertension, but there was a 13% non-significantly higher risk in the larger subset of 1190 patients with hypertension.[5] Although this difference was not statistically significant, these findings suggested that the association between SBP and mortality in HFpEF may be weaker in those with a history of hypertension, which is now confirmed by the findings from the current propensity score-matched study. It is not clear why the presence of hypertension would attenuate the association of SBP with mortality in HFpEF. Hypertension is associated with increased afterload and the resultant increase in

left ventricular end-systolic stiffness (elastance) and left ventricular contractility attenuate the drop of SBP in these patients.[28] However, it has been suggested that in patients with hypertension and HFpEF, the increased stiffness is not accompanied by an associated increase in contractility.[28] This differential increase in stiffness versus contractility is not likely to fully explain the differential association of SBP with mortality in older patients with hypertension,[21] versus in older patients with HFpEF and hypertension (the current study). Because the association between a lower SBP and death was significantly higher in the subgroup discharged on antihypertensive drugs, it is tempting to speculate that a background therapy with antihypertensive drugs may have modified the association. However, findings from subgroup analyses based on prevalent users of antihypertensive drugs need to be interpreted with caution.[30]

According to the 2017 update of the heart failure guideline, patients with HFpEF and persistent hypertension should be treated with guideline-directed medical therapy (GDMT) to attain SBP <130 mmHg after the management of volume overload.[31] Patients in our study were hospitalized with decompensated heart failure and likely had fluid overload. Although acute volume overload is expected to be corrected before hospital discharge, a substantial proportion of patients may still be discharged with some degree of volume overload.[32] It is unknown, however, if the association of SBP <130 mmHg with outcomes in patients with HFpEF and hypertension may vary by volume status. Currently, there is no randomized controlled trial evidence to support a target SBP goal or that lowering SBP improves outcomes in patients with HFpEF and hypertension. In the PARAGON-HF (Prospective Comparison of ARNI With ARB Global Outcomes in HF With Preserved Ejection Fraction) trial in which over 95% of the patients with HFpEF had a history of hypertension, compared with patients receiving valsartan alone, those receiving sacubitril/valsartan had significantly lower SBP by about 5 mmHg at 4 weeks, regardless of baseline SBP.[33] However, this greater reduction in SBP did not translate into improved outcomes.[33, 34] Furthermore, after 4 weeks of therapy with sacubitril/valsartan, there was an increase in SBP in patients whose baseline SBP was already controlled (<130 mmHg).[33] Future randomized controlled trials are needed to determine optimal target goals for blood pressure in patients with HFpEF and uncontrolled hypertension. Future studies also need to examine whether physical activity may improve outcomes in patients with HFpEF and hypertension.[35–38] Although findings of subgroup analysis need to be interpreted with caution,[30] the association of SBP with outcomes in African American patients with HFpEF and hypertension needs to be investigated in larger cohorts as the higher risk among African Americans may be a reflection of differences in the pathogenesis and prognosis of hypertension among African Americans.[39–41]

Study Limitations

As in any observational study, significant associations may be due to residual confounding of measured baseline characteristics or confounding by an unmeasured baseline characteristic. Findings from our sensitivity analyses suggest that the significant associations observed in our study could be relatively sensitive to hidden bias. However, to be a confounder, an unmeasured baseline characteristic would need to be a near-perfect predictor of death and not be strongly associated with any of the 66 baseline characteristics used

in our study. It has been suggested because a lower achieved blood pressure, such as the discharge SBP used in our study, is often associated with favorable baseline health characteristics, and hence observed associations are likely to be favorable, and confounded.[42] However, that is unlikely to explain our results as we observed a higher risk of death associated with lower achieved SBP. We had no data on post-discharge SBP, and SBP cross-over during follow-up may have diluted some of the observed associations. Finally, our data based on fee-for-service Medicare beneficiaries may limit generalizability.

Conclusions

About half of the older patients with HFpEF and a history of hypertension had a discharge SBP within the recommended target of <130 mmHg. However, we found no evidence that these patients had better outcomes compared to those with uncontrolled higher SBP. About a third of the patients had discharge SBP <120 mmHg, and these patients had a significantly higher risk of death, but not of readmission. These findings highlight the need for prospective studies to evaluate optimal SBP treatment goals in patients with HFpEF and hypertension.

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Clinical Significance

- Among hospitalized older patients with heart failure with preserved ejection fraction (HFpEF) and hypertension, a systolic blood pressure (SBP) <130 mmHg was not associated with a higher risk of all-cause mortality compared to SBP ≥130 mmHg.
- However, SBP <120 mmHg was associated with a higher risk of all-cause mortality but not of readmission compared to SBP ≥130 mmHg.
- Future prospective studies need to evaluate optimal SBP treatment goals among patients with HFpEF and hypertension.

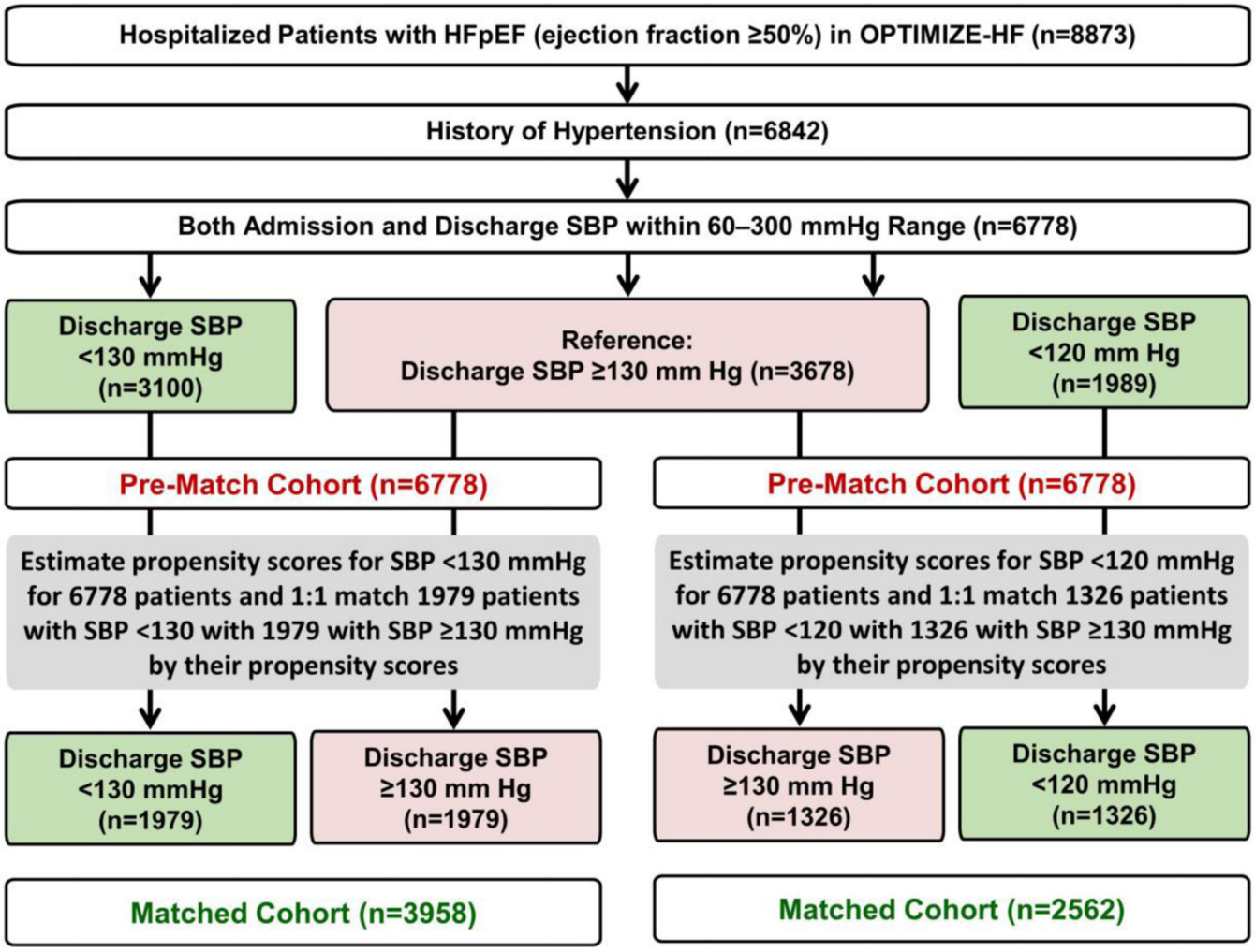

Figure 1.

Flow chart displaying assembly of propensity score matched cohorts of patients with HFpEF and a history of hypertension with discharge SBP ≥130 vs. <130 mm Hg (left panel) and discharge SBP ≥130 vs. <120 mmHg (right panel). HFpEF = heart failure and left ventricular ejection fraction; OPTIMIZE-HF = Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure; SBP = systolic blood pressure.

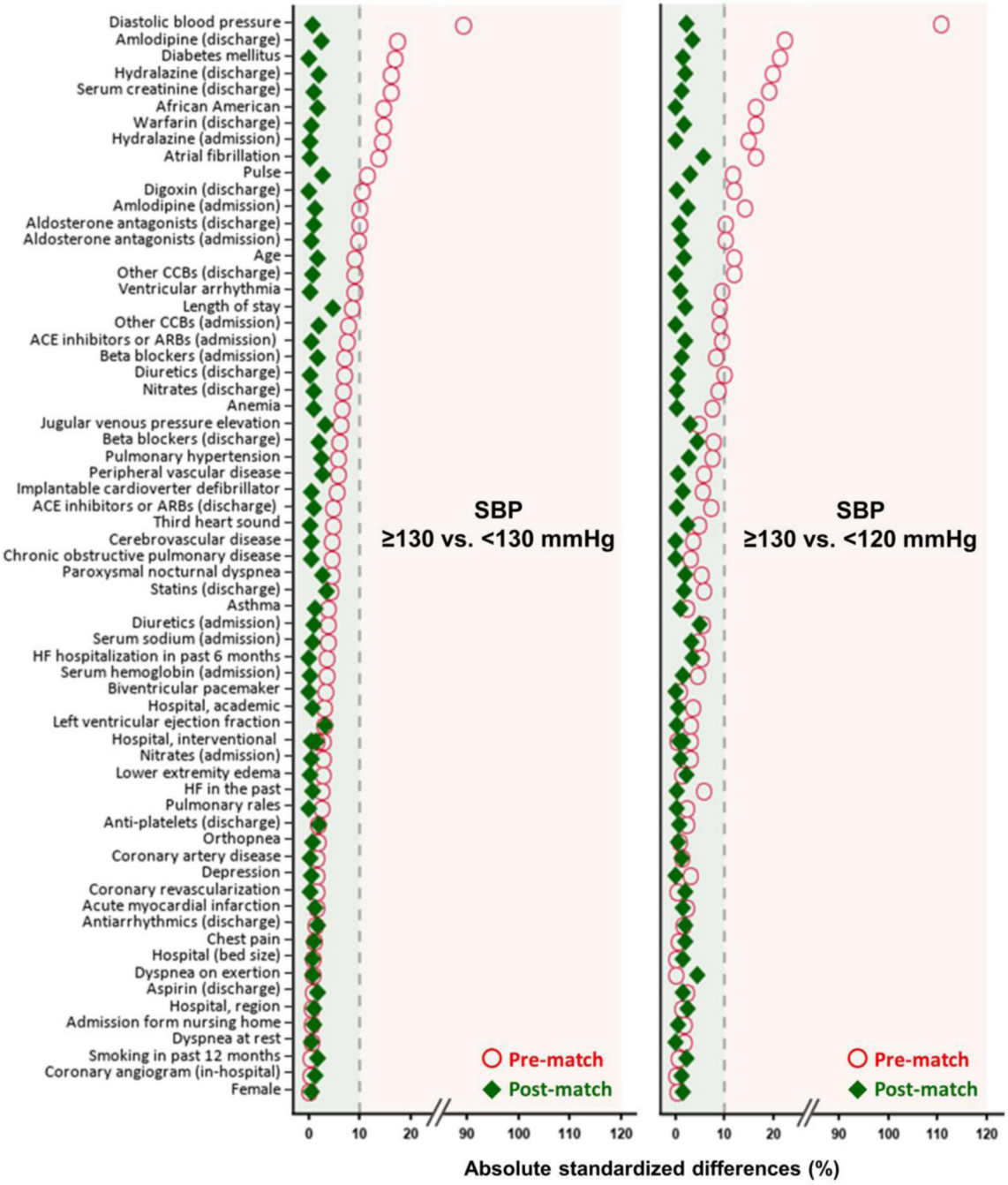

Figure 2.

Love plot displaying balance in 66 baseline characteristics in patients with HFpEF and hypertension between those with a discharge SBP≥130 vs. <130 mmHg (left panel) and those with a discharge SBP≥130 vs. <120 mmHg (right panel) before and after propensity score matching. HFpEF = heart failure and left ventricular ejection fraction; SBP = systolic blood pressure.

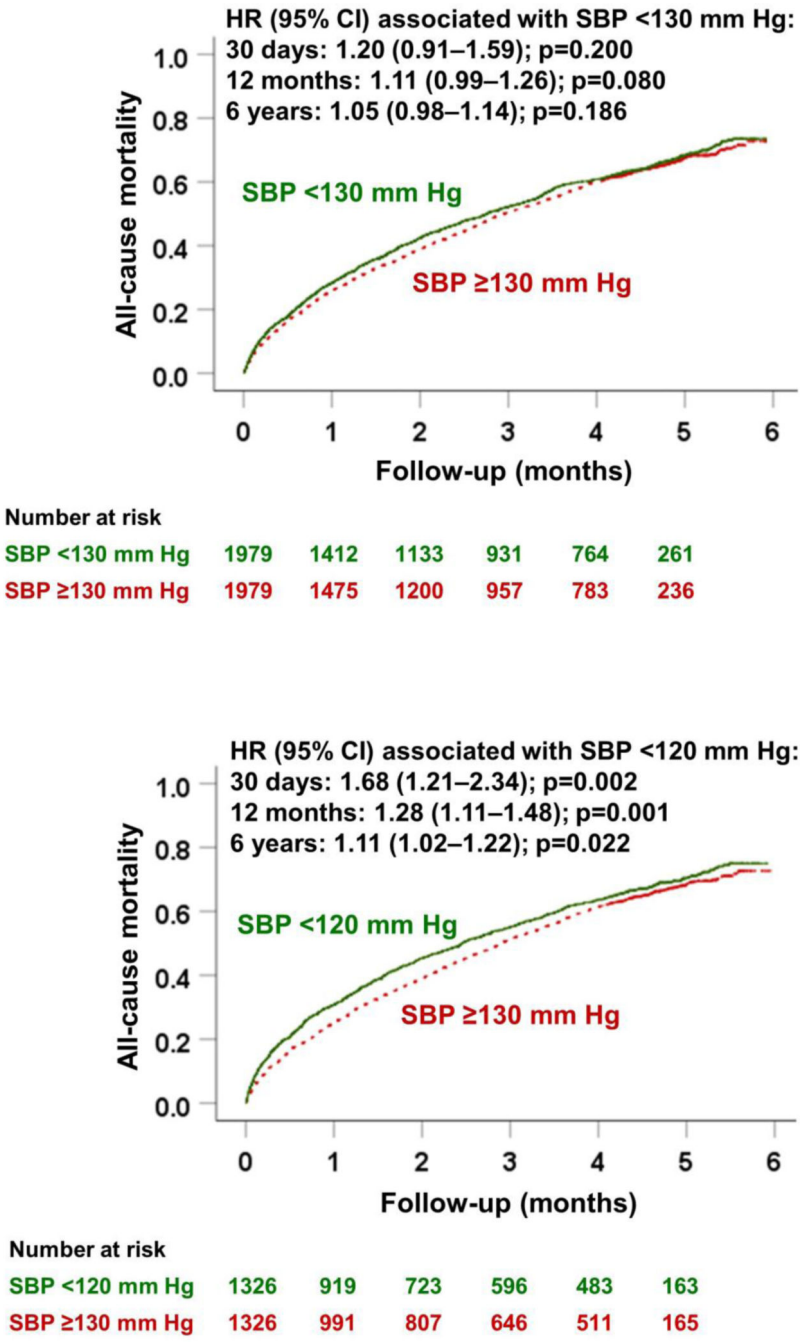

Figure 3.

Kaplan-Meier plots displaying associations of discharge SBP <130 versus ≥130 mm Hg (top panel) and <120 versus ≥130 mm Hg (bottom panel) with all-cause mortality in two separate propensity score-matched cohorts of patients with HFpEF and hypertension. CI = confidence interval; HFpEF = heart failure with preserved ejection fraction; HR = hazard ratio; SBP = systolic blood pressure.

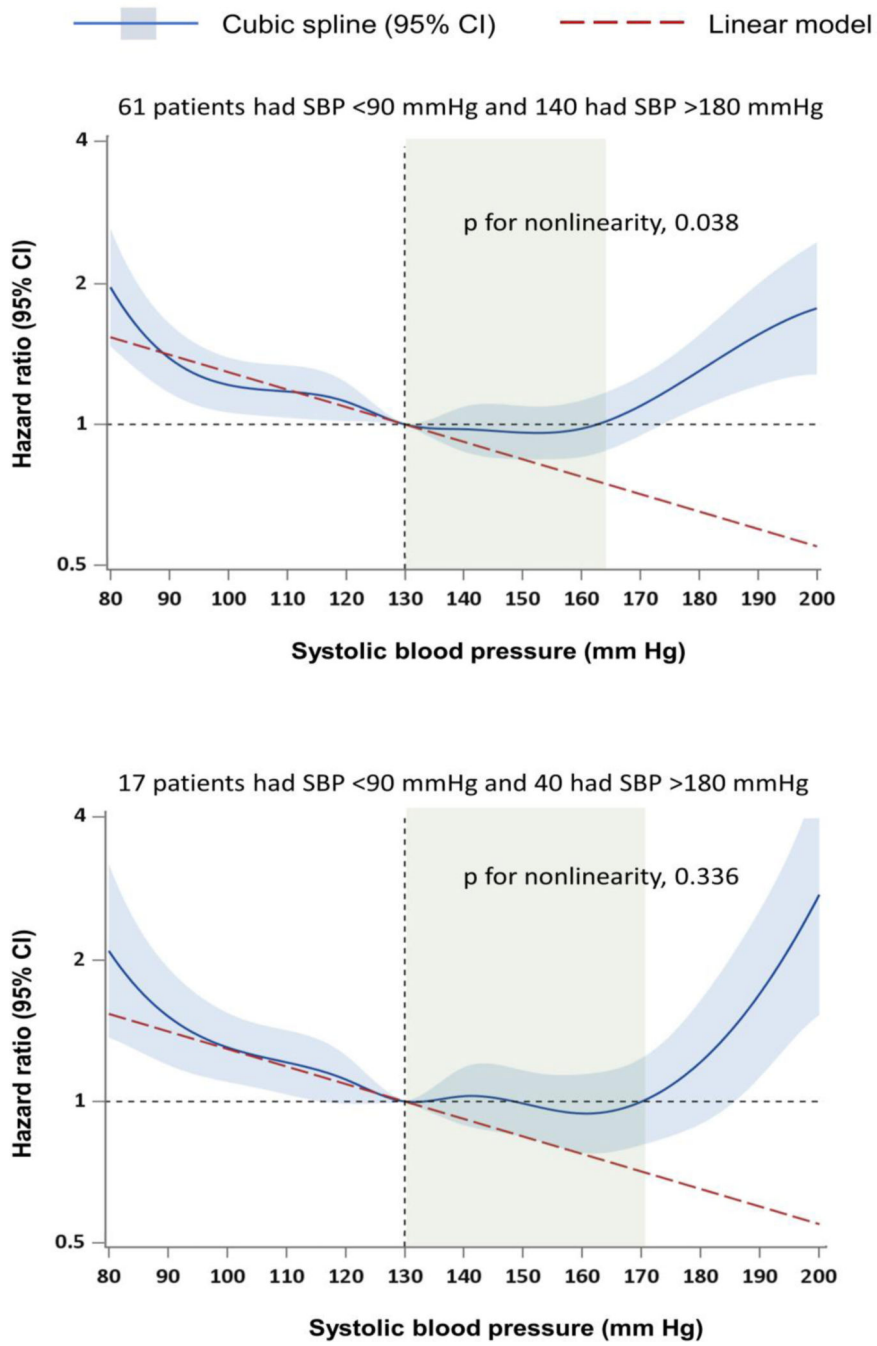

Figure 4.

Restricted cubic spline plots for discharge SBP and 6-year all-cause mortality by in patients with HFpEF and hypertension, among 6,778 pre-match patients, adjusted for propensity scores (non-linearity p = 0.038; top), and among 3,958 propensity score-matched patients balanced on 66 baseline characteristics (non-linearity p = 0.336; bottom) Solid blue lines represent hazard ratios, and blue shaded areas represent 95% CIs. CI =confidence intervals; HFpEF = heart failure with preserved ejection fraction; SBP = systolic blood pressure.

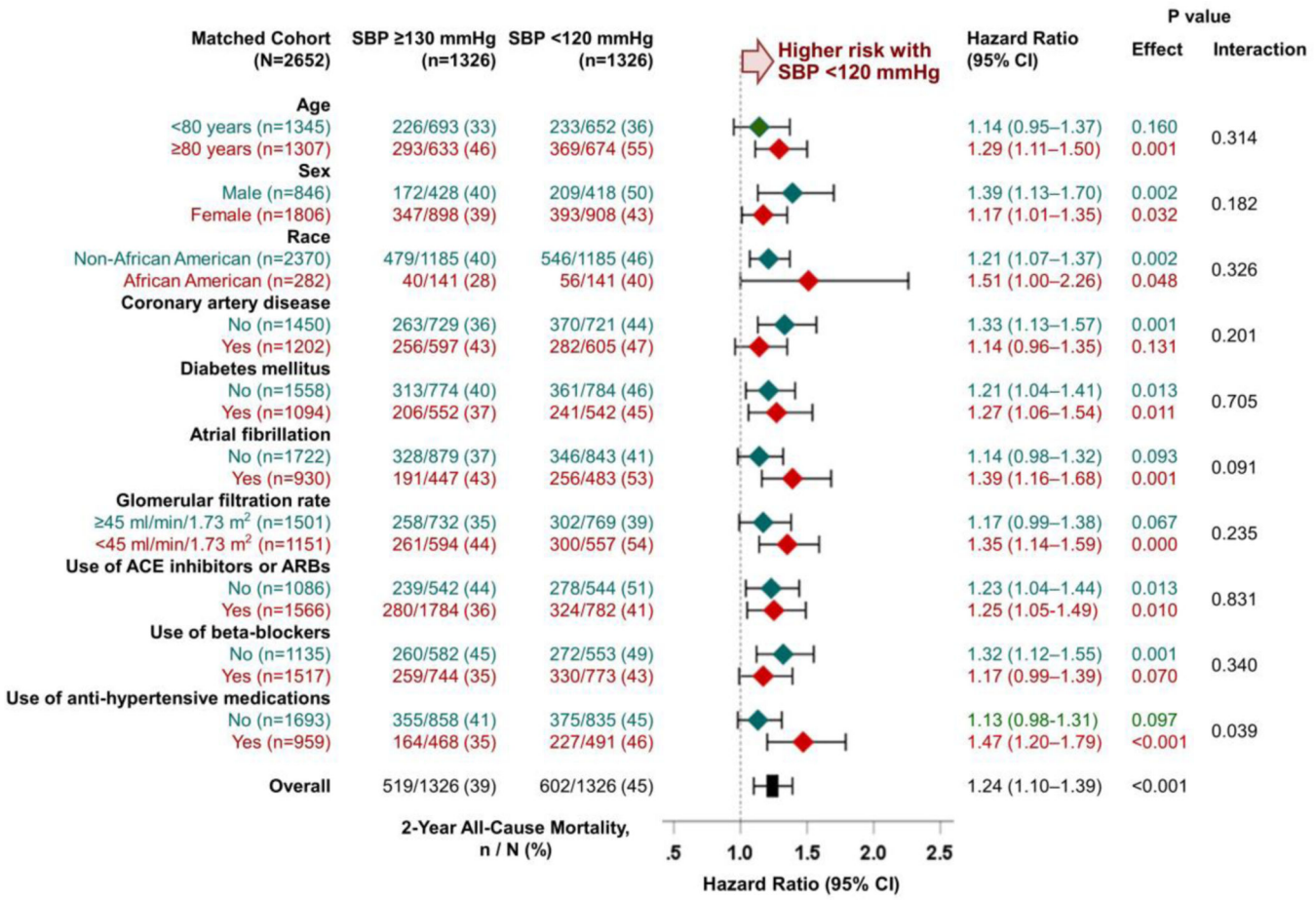

Figure 5.

Forest plots displaying associations of SBP <120 (versus ≥130 mmHg) with 2-year all-cause mortality in subgroups of patients with HFpEF and hypertension. ACE = angiotensin-converting enzyme, ARB = angiotensin receptor blocker, CI = confidence interval; HFpEF = heart failure and left ventricular ejection fraction; SBP = systolic blood pressure. Note: Results of subgroup analyses need to be interpreted with caution as they may be false-positive due to multiple comparisons and false-negative due to inadequate power.

Table 1.

Baseline Characteristics of Patients with HFpEF and Hypertension with SBP ≥130 mmHg vs. <130 mmHg

n (%) or mean (SD)	Pre-propensity score matching (n=6778)			Post-propensity score matching (n=3958)		
	Discharge SBP			Discharge SBP		
	≥130 mmHg (n=3678)	<130 mmHg (n=3100)	P value	≥130 mmHg (n=1979)	<130 mmHg (n=1979)	P value
Age (years)	77.6 (±10.7)	78.6 (±10.6)	<0.001	78.6 (±9.8)	78.4 (±10.7)	0.570
Female	2496 (68%)	2104 (68%)	0.994	1363 (69%)	1357 (69%)	0.837
African American	586 (16%)	339 (11%)	<0.001	247 (12%)	235 (12%)	0.560
Left ventricular ejection fraction (%)	57.1 (±6.3)	57.0 (±6.2)	0.224	57.2 (±6.3)	56.9 (±6.2)	0.287
Past medical history						
HF in the past	3163 (86%)	2694 (87%)	0.278	1716 (87%)	1710 (86%)	0.780
HF hospitalization in past 6 months	373 (10%)	348 (11%)	0.149	196 (10%)	196 (10%)	1.000
Coronary artery disease	1624 (44%)	1393 (45%)	0.519	872 (44%)	870 (44%)	0.949
Atrial fibrillation	1108 (30%)	1132 (37%)	<0.001	673 (34%)	676 (34%)	0.920
Pulmonary hypertension	281 (8%)	286 (9%)	0.019	164 (8%)	178 (9%)	0.428
Cerebrovascular disease	699 (19%)	534 (17%)	0.059	359 (18%)	354 (18%)	0.836
Peripheral vascular disease	595 (16%)	439 (14%)	0.021	283 (14%)	303 (15%)	0.371
Diabetes mellitus	1746 (47%)	1213 (39%)	<0.001	851 (43%)	851 (43%)	1.000
Chronic obstructive pulmonary disease	1033 (28%)	934 (30%)	0.065	588 (30%)	582 (29%)	0.834
Anemia	856 (23%)	639 (21%)	0.008	422 (21%)	413 (21%)	0.726
Depression	458 (12%)	402 (13%)	0.525	244 (12%)	248 (13%)	0.847
Admission clinical findings						
Dyspnea on exertion	2330 (63%)	1952 (63%)	0.745	1250 (63%)	1242 (63%)	0.792
Orthopnea	961 (26%)	834 (27%)	0.471	518 (26%)	511 (26%)	0.800
Paroxysmal nocturnal dyspnea	537 (15%)	405 (13%)	0.069	255 (13%)	274 (14%)	0.375
Dyspnea at rest	1583 (43%)	1324 (43%)	0.784	836 (42%)	841 (42%)	0.872
Jugular venous pressure elevation	904 (25%)	847 (27%)	0.010	511 (26%)	539 (27%)	0.313
Pulmonary rales	2355 (64%)	2023 (65%)	0.292	1294 (65%)	1293 (65%)	0.973
Lower extremity edema	2433 (66%)	2090 (67%)	0.269	1319 (67%)	1321 (67%)	0.946
Systolic blood pressure (mmHg) *	161 (±33.2)	144 (±30.8)	<0.001	158 (±32.5)	145 (±30.4)	<0.001
Admission medications						
ACE inhibitors or ARBs	1927 (52%)	1509 (49%)	0.002	998 (50%)	1004 (51%)	0.849
Beta blockers	2064 (56%)	1631 (53%)	0.004	1039 (53%)	1056 (53%)	0.588
Aldosterone antagonists	110 (3%)	150 (5%)	<0.001	69 (3%)	71 (4%)	0.863
Diuretics	2326 (63%)	2016 (65%)	0.126	1281 (65%)	1270 (64%)	0.715
Hydralazine	140 (4%)	47 (2%)	<0.001	40 (2%)	41 (2%)	0.911

n (%) or mean (SD)	Pre-propensity score matching (n=6778)			Post-propensity score matching (n=3958)		
	Discharge SBP			Discharge SBP		
	≥130 mmHg (n=3678)	<130 mmHg (n=3100)	P value	≥130 mmHg (n=1979)	<130 mmHg (n=1979)	P value
Nitrates	793 (22%)	634 (20%)	0.265	410 (21%)	415 (21%)	0.845
Amlodipine	556 (15%)	364 (12%)	<0.001	256 (13%)	264 (13%)	0.707
Other CCBs	799 (22%)	577 (19%)	0.002	409 (21%)	392 (20%)	0.501
Discharge clinical findings						
Pulse (beats/minute)	73.2 (±13.5)	74.7 (±13.7)	<0.001	74.4 (±13.8)	74.0 (±13.3)	0.382
Systolic blood pressure (mmHg) *	148 (±14.6)	113 (±10.8)	<0.001	145 (±12.9)	115 (±10.0)	<0.001
Diastolic blood pressure (mmHg)	71.0 (±11.9)	61.0 (±10.4)	<0.001	64.9 (±10.1)	64.9 (±9.6)	0.796
Serum creatinine (mg/dL)	1.9 (±1.5)	1.6 (±1.3)	<0.001	1.7 (±1.2)	1.7 (±1.4)	0.724
Discharge medications						
ACE inhibitors or ARBs	2251 (61%)	1824 (59%)	0.048	1168 (59%)	1178 (60%)	0.746
Beta blockers	2278 (62%)	1830 (59%)	0.015	1158 (59%)	1179 (60%)	0.497
Aldosterone antagonists	228 (6%)	272 (9%)	<0.001	144 (7%)	150 (8%)	0.716
Digoxin	540 (15%)	575 (19%)	<0.001	327 (17%)	328 (17%)	0.966
Diuretics	2852 (78%)	2492 (80%)	0.004	1566 (79%)	1568 (79%)	0.938
Hydralazine	205 (6%)	75 (2%)	<0.001	72 (4%)	65 (3%)	0.543
Nitrates	997 (27%)	749 (24%)	0.006	519 (26%)	509 (26%)	0.717
Amlodipine	604 (16%)	326 (11%)	<0.001	231 (12%)	247 (12%)	0.435
Other CCBs	770 (21%)	540 (17%)	<0.001	394 (20%)	387 (20%)	0.780
Length of stay (days)	5.5 (±4.5)	5.9 (±5.1)	<0.001	5.8 (±4.9)	5.6 (±4.2)	0.140
Hospital, bed size	393 (±242)	391 (±236)	0.738	392 (±245)	390 (±241)	0.827

* SBP is the exposure variable and would not be expected to be imbalanced in the matched cohort; presented for descriptive purposes only.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CCB = calcium channel blockers; COPD = chronic obstructive pulmonary disease; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; SBP = systolic blood pressure

Table 2.

Baseline Characteristics of Patients with HFpEF and Hypertension with SBP ≥130 mmHg vs. <120 mmHg

n (%) or mean (SD)	Pre-propensity score matching (n=5667)			Post-propensity score matching (n=2652)		
	Discharge SBP			Discharge SBP		
	≥130 mmHg (n=3678)	<120 mmHg (n=1989)	P value	≥130 mmHg (n=1326)	<120 mmHg (n=1326)	P value
Age (years)	77.6 (±10.7)	78.9 (±10.4)	<0.001	78.8 (±9.6)	79.0 (±10.2)	0.628
Female	2496 (68%)	1346 (68%)	0.883	898 (68%)	908 (68%)	0.677
African American	586 (16%)	208 (10%)	<0.001	141 (11%)	141 (11%)	1.000
Left ventricular ejection fraction (%)	57.1 (±6.3)	56.9 (±6.3)	0.277	57.0 (±6.3)	56.9 (±6.4)	0.953
Past medical history						
HF in the past	3163 (86%)	1749 (88%)	0.041	1163 (88%)	1162 (88%)	0.953
HF hospitalization in past 6 months	373 (10%)	235 (12%)	0.052	134 (10%)	148 (11%)	0.378
Coronary artery disease	1624 (44%)	892 (45%)	0.617	597 (45%)	605 (46%)	0.755
Atrial fibrillation	1108 (30%)	753 (38%)	<0.001	447 (34%)	483 (36%)	0.143
Pulmonary hypertension	281 (8%)	193 (10%)	0.007	121 (9%)	132 (10%)	0.467
Cerebrovascular disease	699 (19%)	351 (18%)	0.209	243 (18%)	244 (18%)	0.960
Peripheral vascular disease	595 (16%)	281 (14%)	0.042	208 (16%)	211 (16%)	0.873
Diabetes mellitus	746 (47%)	736 (37%)	<0.001	552 (42%)	542 (41%)	0.693
Chronic obstructive pulmonary disease	1033 (28%)	585 (29%)	0.292	394 (30%)	393 (30%)	0.966
Anemia	856 (23%)	401 (20%)	0.007	282 (21%)	280 (21%)	0.924
Depression	458 (12%)	268 (13%)	0.272	167 (13%)	167 (13%)	1.000
Admission clinical findings						
Dyspnea on exertion	2330 (63%)	1260 (63%)	0.999	823 (62%)	852 (64%)	0.243
Orthopnea	961 (26%)	526 (26%)	0.796	348 (26%)	344 (26%)	0.860
Paroxysmal nocturnal dyspnea	537 (15%)	254 (13%)	0.058	190 (14%)	181 (14%)	0.614
Dyspnea at rest	1583 (43%)	839 (42%)	0.533	555 (42%)	554 (42%)	0.969
Jugular venous pressure elevation	904 (25%)	531 (27%)	0.080	328 (25%)	346 (26%)	0.422
Pulmonary rales	2355 (64%)	1296 (65%)	0.397	858 (65%)	860 (65%)	0.935
Lower extremity edema	2433 (66%)	1328 (67%)	0.639	875 (66%)	889 (67%)	0.565
Systolic blood pressure (mmHg) *	161 (±33.2)	141 (±30.1)	<0.001	158 (±32.6)	141 (±29.9)	<0.001
Admission medications						
ACE inhibitors or ARBs	1927 (52%)	949 (48%)	<0.001	662 (50%)	649 (49%)	0.614
Beta blockers	2064 (56%)	1036 (52%)	0.004	682 (51%)	690 (52%)	0.756
Aldosterone antagonists	110 (3%)	99 (5%)	<0.001	51 (4%)	48 (4%)	0.759
Diuretics	2326 (63%)	1309 (66%)	0.054	850 (64%)	882 (67%)	0.192
Hydralazine	140 (4%)	29 (1%)	<0.001	25 (2%)	25 (2%)	1.000

n (%) or mean (SD)	Pre-propensity score matching (n=5667)			Post-propensity score matching (n=2652)		
	Discharge SBP			Discharge SBP		
	≥130 mmHg (n=3678)	<120 mmHg (n=1989)	P value	≥130 mmHg (n=1326)	<120 mmHg (n=1326)	P value
Nitrates	793 (22%)	405 (20%)	0.292	266 (20%)	271 (20%)	0.809
Amlodipine	556 (15%)	207 (10%)	<0.001	149 (11%)	160 (12%)	0.506
Other CCBs	799 (22%)	362 (18%)	0.002	268 (20%)	267 (20%)	0.961
Discharge clinical findings						
Pulse (beats/minute)	73.2 (±13.5)	74.8 (±13.8)	<0.001	73.7 (±13.7)	74.2 (±13.4)	0.445
Systolic blood pressure (mmHg) *	148 (±14.6)	107 (±8.7)	<0.001	144 (±12.1)	108 (±8.0)	<0.001
Diastolic blood pressure (mmHg)	71.0 (±11.9)	59.0 (±9.6)	<0.001	62.1 (±9.5)	62.3 (±8.8)	0.535
Serum creatinine (mg/dL)	1.9 (±1.5)	1.6 (±1.2)	<0.001	1.7 (±1.3)	1.6 (±1.3)	0.740
Discharge medications						
ACE inhibitors or ARBs	2251 (61%)	1146 (58%)	0.009	784 (59%)	782 (59%)	0.937
Beta blockers	2278 (62%)	1158 (58%)	0.006	744 (56%)	773 (58%)	0.255
Aldosterone antagonists	228 (6%)	177 (9%)	<0.001	96 (7%)	99 (7%)	0.823
Digoxin	540 (15%)	380 (19%)	<0.001	228 (17%)	229 (17%)	0.959
Diuretics	2852 (78%)	1622 (82%)	<0.001	1058 (80%)	1061 (80%)	0.884
Hydralazine	205 (6%)	37 (2%)	<0.001	30 (2%)	34 (3%)	0.613
Nitrates	997 (27%)	465 (23%)	0.002	324 (24%)	322 (24%)	0.928
Amlodipine	604 (16%)	181 (9%)	<0.001	136 (10%)	150 (11%)	0.381
Other CCBs	770 (21%)	324 (16%)	<0.001	245 (18%)	244 (18%)	0.960
Length of stay (days)	5.5 (±4.5)	5.9 (±5.4)	<0.001	5.7 (±4.7)	5.8 (±4.7)	0.610
Hospital, bed size	393 (±242)	393 (±230)	0.995	396 (±255)	392 (±234)	0.697

* SBP is the exposure variable and would not be expected to be imbalanced in the matched cohort; presented for descriptive purposes only. ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CCB = calcium channel blockers; COPD = chronic obstructive pulmonary disease; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; SBP = systolic blood pressure

Table 3.

Outcomes by Discharge SBP <130 (Versus ≥130 mmHg; Upper Panel) and <120 (Versus ≥130 mmHg; Lower Panel) in Propensity Score–Matched Cohorts of Patients with HFpEF and Hypertension

Outcomes by Duration of Follow-up	Events (%), by		HR (95% CI); p value
	Discharge SBP ≥130 mmHg (n=1979)	Discharge SBP <130 mmHg (n=1979)	Associated with SBP <130 mmHg
All-cause mortality			
30 days	89 (4.5%)	107 (5.4%)	1.20 (0.91–1.59); p=0.200
12 months	513 (26%)	560 (28%)	1.11 (0.99–1.26); p=0.080
6 years	1314 (66%)	1341 (68%)	1.05 (0.98–1.14); p=0.186
All-cause readmission			
30 days	434 (22%)	453 (23%)	1.05 (0.92–1.20); p=0.487
12 months	1310 (66%)	1347 (68%)	1.06 (0.99–1.15); p=0.115
6 years	1754 (89%)	1740 (88%)	1.03 (0.97–1.10); p=0.334
Heart failure readmission			
30 days	145 (7.3%)	146 (7.4%)	1.01 (0.80–1.27); p=0.945
12 months	558 (28%)	566 (29%)	1.03 (0.92–1.16); p=0.613
6 years	896 (45%)	901 (46%)	1.03 (0.94–1.13); p=0.525
	Discharge SBP ≥130 mmHg (n=1326)	Discharge SBP <120 mmHg (n=1326)	Associated with SBP <120 mmHg
All-cause mortality			
30 days	56 (4.2%)	93 (7.0%)	1.68 (1.21–2.34); p=0.002
12 months	335 (25%)	407 (31%)	1.28 (1.11–1.48); p=0.001
6 years	896 (68%)	929 (70%)	1.11 (1.02–1.22); p=0.022
All-cause readmission			
30 days	322 (24%)	308 (23%)	0.97 (0.83–1.13); p=0.690
12 months	897 (68%)	896 (68%)	1.05 (0.96–1.15); p=0.317
6 years	1184 (89%)	1156 (87%)	1.02 (0.94–1.11); p=0.613
Heart failure readmission			
30 days	106 (8.0%)	101 (7.6%)	0.97 (0.74–1.27); p=0.809
12 months	389 (29%)	379 (29%)	1.01 (0.88–1.17); p=0.851
6 years	622 (47%)	595 (45%)	1.00 (0.89–1.12); p=0.992

* Considering that formal sensitivity analyses can only be conducted when associations are significant in the matched cohort and because the association of discharge SBP <120 mmHg with all-cause mortality was consistently significant at all 3 timepoints, formal sensitivity analyses were limited to this outcome. Of the 1326 matched pairs of patients with SBP <120 vs ≥130 mmHg, in 143 pairs we were able to determine which patient within a pair clearly had a longer 30-day survival and fewer (39% or 55/143) of those patients belonged to the SBP <120 (vs. ≥130) mmHg group (sign-score test P=0.020). A hidden covariate could explain away this association if it increased the odds of having SBP <120 mmHg by 12.6%. Respective numbers for 12-month and 6-year mortality were 8.6% and 1.2%. CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.