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Association of Blood Pressure at Hospital Discharge With Mortality in Patients Diagnosed With Heart Failure

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Background—Higher blood pressure in acute heart failure has been associated with improved survival; however, the relationship between blood pressure and survival in stabilized patients at hospital discharge has not been established.

Methods and Results—In 7448 patients with heart failure (75.2 ± 11.5 years; 49.9% men) discharged from the hospital in Ontario, Canada, we examined the association of systolic blood pressure (SBP) and diastolic blood pressure with long-term survival. Parametric survival analysis was performed, and survival time ratios were determined according to discharge blood pressure group. A total of 25 427 person-years of follow-up were examined. In those with left ventricular ejection fraction $\leq 40\%$, median survival was decreased by 17% (survival time ratio, 0.83; 95% CI, 0.71 to 0.98; $P=0.029$) when discharge SBP was 100 to 119 mm Hg and decreased by 23% (survival time ratio, 0.77; 95% CI, 0.62 to 0.97; $P=0.024$) when discharge SBP was <100 mm Hg, compared with those in the reference range of 120 to 139 mm Hg. Survival time ratios were 0.75 (95% CI, 0.60 to 0.92; $P=0.007$) and 0.75 (95% CI, 0.53 to 1.07; $P=0.12$) when discharge SBPs were 140 to 159 and ≥ 160 mm Hg, respectively. In those with left ventricular ejection fraction $>40\%$, survival time ratios were 0.69 (95% CI, 0.51 to 0.93), 0.83 (95% CI, 0.71 to 0.99), 0.95 (95% CI, 0.80 to 1.14), and 0.76 (95% CI, 0.61 to 0.95) for discharge SBPs <100 , 100 to 119, 140 to 159, and ≥ 160 mm Hg, respectively.

Conclusions—In this long-term population-based study of patients with heart failure, the association of discharge SBP with mortality followed a U-shaped distribution. Survival was shortened in those with reduced or increased values of discharge SBP. (*Circ Heart Fail.* 2009;2:616-623.)

Key Words: heart failure ■ blood pressure ■ hypertension ■ mortality ■ health outcomes

Heart failure (HF) is associated with a high mortality rate and is a leading cause of hospitalization. Each year, in the United States, $>500\,000$ patients with acute HF are admitted to the hospital, and they are treated for the acute episode transitioning to chronic HF at discharge. At the time of acute HF onset, the blood pressure at initial presentation has been shown to be a strong predictor of early death.^{1,2} Acute hemodynamic perturbations at the time of hospital presentation are related, in part, to underlying left ventricular systolic performance or the peripheral vascular milieu, and both may reflect the initial blood pressure at acute HF onset. However, there is a paucity of knowledge about the relationship between blood pressure in nonacute HF and long-term survival.

Clinical Perspective on p 623

Guidelines for both hypertension and HF care do not provide optimal blood pressure goals for the management of

patients with HF overall or in those with reduced or preserved left ventricular ejection fraction (LVEF).³ Indeed, recent disease-specific guidelines on long-term management of patients with stage 3 HF recommend achievement of blood pressure targets that are applicable to hypertensive patients in general, and there are no suggested lower or upper blood pressure limits that indicate prognostic concern.^{4,5} This may, in part, be due to the seemingly paradoxical inverse relationship of blood pressure and survival in patients with HF.^{6,7}

The blood pressure at the time of hospital discharge is an early assessment of the ambulatory clinic blood pressure; however, the importance of this variable in those with established HF has not been determined. Evaluation of the effect of blood pressure on mortality in community patients with chronic HF would require long-term follow-up and consideration of prevalent comorbidities, with the attendant potential for death due to competing risks from noncardiac

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causes potentially abrogating the effect of blood pressure on survival.⁸ Although data from previous studies have suggested that lower blood pressure increases the risk of death,^{9–11} the effect of this parameter over a broad range of measurements has not been assessed. Furthermore, the effect of blood pressure at the time of hospital discharge on long-term survival has not been evaluated in a population-based setting.

In this study, we examined the effect of discharge blood pressures on long-term survival in a community-based sample of stabilized patients with HF. We hypothesized that a U-shaped relationship would be present such that discharge blood pressures deviating toward high or low values would confer significantly increased risk of death.

Methods

Patients

We examined patients with HF in the Enhanced Feedback For Effective Cardiac Treatment Heart Failure (EFFECT-HF) study who were discharged alive after presenting with decompensated HF to an acute care hospital. The EFFECT-HF cohort is a population-based sample of patients with HF, defined by the modified Framingham criteria,¹² admitted to any of the 103 acute care hospitals in Ontario, Canada, from April 1, 1999, to March 30, 2001. Detailed clinical data collection, including clinical characteristics, general and cardiac laboratory investigations, and treatments in hospital, was performed from hospital records.^{1,13}

Primary Outcome and Data Sources

The primary study end point was death from any cause after the index HF hospital discharge. We linked the clinical data from the EFFECT-HF Study with the Registered Persons Database for determination of vital status and the Canadian Institute for Health Information database for in-hospital deaths. Linkages of clinical and administrative data were performed using the unique, encrypted health card number. The accuracy of the data in these databases has been previously described.^{13–15} Ethical approval was obtained from all participating institutions before data collection and linkage.

Clinical Categorization of Blood Pressures and LVEF

Hospital medical records were abstracted by highly trained nurse chart abstractors. Discharge blood pressure was the last recorded blood pressure obtained within 24 hours before or at hospital discharge, whereas admission blood pressure was the first recorded measurement in the emergency department.¹ Discharge systolic blood pressures (SBPs) and diastolic blood pressures (DBPs) were categorized based on standard clinical groupings.^{3,4} The use of these clinical groupings was consistent with an analysis in which the nature of the relationship between blood pressure and the log odds of death was examined using cubic spline functions.¹⁶ LVEF was determined from the echocardiogram, radionuclide angiogram, or cardiac catheterization procedures performed during the hospital stay. Reduced and preserved systolic function were defined by LVEF $\leq 40\%$ versus $>40\%$, respectively.

Statistical Analysis

Demographic and clinical characteristics of patients according to discharge SBP and DBP were compared using the χ^2 test and ANOVA for dichotomous and continuous variables, respectively. Correlations were examined using the Pearson R^2 statistic. To categorize blood pressure into 5 groups, we examined the shape of the association between SBPs and DBPs with 1-year mortality adjusting for all EFFECT-HF risk covariates using cubic spline analysis for Cox regression with knots at the 5th, 27.5th, 50th, 72.5th, and 95th percentiles.¹⁶

Modeling of long-term survival was not performed with Cox proportional hazards regression analysis because there was a violation of the assumption of proportionality of hazards that was confirmed using Schoenfeld residuals.¹⁷ We therefore used a parametric accelerated failure time survival model with a generalized γ distribution to model the impact of discharge blood pressure on survival time in all patients and in those with reduced ejection fraction.¹⁸ For those with LVEF $>40\%$, the generalized γ distribution model did not converge, and thus, the Weibull survival model was used. Long-term survival in different blood pressure categories was compared relative with the referent group with discharge blood pressure in the middle range, and the ratios of median survival times were calculated. A survival time ratio <1 indicated shortened survival compared with the reference blood pressure range.

The effects of discharge blood pressure were examined after adjustment for the covariates of the EFFECT-HF mortality risk model,^{19–21} which was found to discriminate long-term mortality.²² The EFFECT-HF risk model covariates include age, admission SBP, anemia, hyponatremia, renal function, presence of chronic lung disease, and several comorbidities, and these were entered as separate covariates, thus allowing for a refitted mortality model in the study cohort.¹ In additional analyses, we further adjusted for other clinical factors that could potentially affect survival, including (i) prior myocardial infarction; (ii) prior stroke or transient ischemic attack; (iii) atrial fibrillation; (iv) diabetes; (v) peptic ulcer disease; (vi) preadmission New York Heart Association functional class; (vii) heart rate and oxygen saturation at presentation; (viii) serum creatinine concentration; and (ix) use of β -adrenoreceptor antagonists, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and diuretics at the time of hospital discharge.

In stratified analyses, we studied patients according to LVEF $\leq 40\%$ versus $>40\%$. Median survival time was determined for patients in different strata of discharge blood pressure and EFFECT-HF risk score to obtain expected survival estimates. Patients were censored at death or on the last follow-up date of March 31, 2007. Continuous variables are reported using mean \pm SD, and survival curves were displayed using the Kaplan–Meier method. A 2-sided P value <0.05 for comparisons was considered statistically significant. All analyses were performed using SAS statistical software version 9.1.3 (SAS Institute, Cary, NC).

Results

Patient Characteristics

A total of 7448 patients, comprising 3720 men (49.9%) and mean age 75.2 ± 11.5 years, with all EFFECT-HF risk model components and discharge blood pressure measured were examined in this study. The cohort was followed up for a total of 25 427 person-years, with a median follow-up duration of 2.87 years (25th to 75th percentile: 0.89 to 6.19). A total of 784 patients died before hospital discharge and were therefore excluded from this analysis. The mean SBPs and DBPs in the study cohort were 125 ± 22 and 68 ± 12 mm Hg, respectively. The mean EFFECT-HF risk score was 98 ± 25 . The study cohort was followed up for a total of 25 427 person-years in survival analyses.

Blood Pressure Categories

The continuous relationships of SBP and DBP with death at 1 year are shown in Figure 1, adjusting for the EFFECT-HF risk model. On the basis of the spline analyses and standard clinical groupings, SBPs were grouped into the following 5 categories: <100 , 100 to 119, 120 to 139, 140 to 159, and ≥ 160 mm Hg, and DBPs were grouped into the following 5 categories: <55 , 55 to 64, 65 to 74, 75 to 84, and ≥ 85 mm Hg.

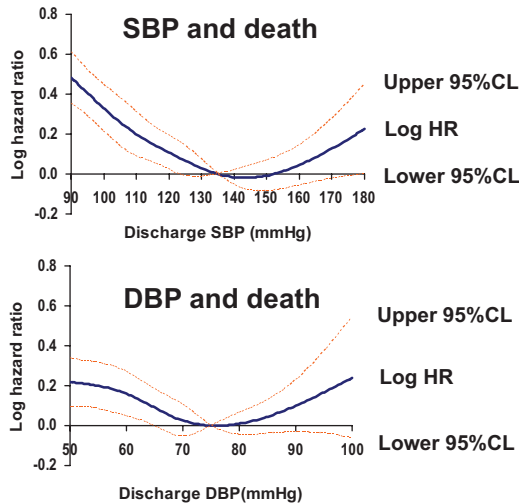


Figure 1. Spline curves relating discharge SBPs and DBPs with mortality, adjusted for EFFECT-HF model covariates and medications. HR indicates hazard ratio; CL, confidence limit.

Discharge SBP was weakly correlated with values at admission (Figure 2), and only a small degree of variation in the former was explained by the latter (Pearson $R^2=0.195$). Discharge DBP was also weakly correlated with admission values, and the degree of variation in the former that was explained by the latter (Pearson $R^2=0.080$) was also small. Similarly, the variations in SBP and DBP that were explained by the EFFECT-HF risk score were also small with Pearson R^2 0.010 and 0.047, respectively.

Correlates of Discharge SBP and DBP

Characteristics of patients according to SBP categories are shown in Table 1. Patients with lower discharge SBP were younger and consisted of more men than those in the higher categories. Patients with lower discharge SBP had more prior myocardial infarction, whereas those in the higher categories had higher rates of diabetes, anemia, and renal insufficiency (Table 1). Lower discharge DBP was associated with older age, whereas higher categories comprised an increased proportion of men (Table 2). Patients with lower discharge DBP had higher prevalence of myocardial infarction, chronic obstructive lung disease, anemia, and hyponatremia at presentation (Table 2). There were no significant interactions between SBP or DBP and the covariates shown in Tables 1 and 2.

Effect of Discharge Blood Pressure on Survival

Kaplan–Meier survival curves by SBP categories are shown in Figure 3. Time-to-event analysis models using the γ distribution adjusting for the EFFECT-HF risk variables are shown in Table 3. The median survival time ratio decreased (eg, the risk of death increased) as the discharge SBP deviated below or above the reference range of 120 to 139 mm Hg. A U-shaped relationship between discharge SBP and mortality was observed when stratified by LVEF. In those with LVEF $\leq 40\%$, there was a 23% reduction in adjusted median survival time in those with SBP <100 mm Hg (survival time ratio, 0.77; 95% CI, 0.62 to 0.97) and a 17% reduction at 100 to 119 mm Hg (survival time ratio, 0.83; 95% CI, 0.71 to

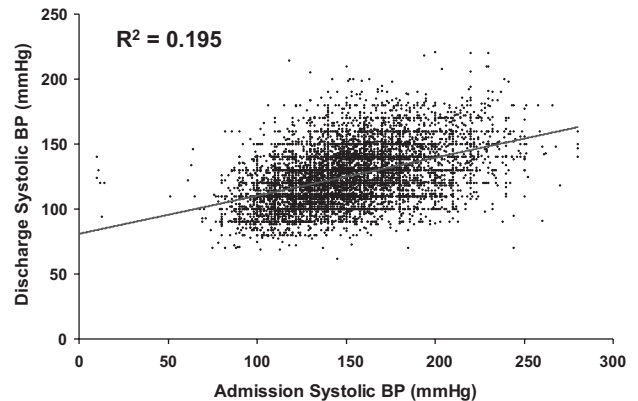


Figure 2. Scatter plots of admission versus discharge SBPs.

0.98) compared with the reference group (Table 3). As the SBP at discharge increased, the median adjusted survival time was 25% lower than that in the reference group (Table 3).

The effect of low SBP on mortality was also observed in those with preserved systolic function. Median survival time decreased by 31% (survival time ratio, 0.69; 95% CI, 0.51 to 0.93) and 17% (survival time ratio, 0.83; 95% CI, 0.71 to 0.99) in those with discharge SBPs <100 and 100 to 119 mm Hg, respectively. A similar U-shaped pattern was also observed with discharge DBP (Table 3). The effects of SBP and DBP were robust even after excluding those with very low SBP (<60 mm Hg) and DBP (<30 mm Hg) from the analysis.

Multivariable Adjusted Analyses

In analyses adjusting for the EFFECT-HF risk model covariates, additional clinical variables, and medications, we found that the U-shaped association between SBP and survival was robust. In those with LVEF $\leq 40\%$, median survival time ratios for discharge SBPs <100 , 100 to 119, 140 to 159, and ≥ 160 mm Hg were reduced by 22% (95% CI, 3 to 38), 17% (95% CI, 2 to 29), 21% (95% CI, 2 to 36), and 21% (95% CI, -13 to 44), respectively. Thus, all SBP ranges (except ≥ 160 mm Hg) conferred a significantly increased risk of death (all $P<0.05$) compared with the reference range (120 to 139 mm Hg).

In patients with LVEF $>40\%$, median survival time ratio was lessened by 29% (95% CI, 4 to 48), 15% (95% CI, 0 to 29), 4% (95% CI, -16 to 20), and 24% (95% CI, 4 to 39) when discharge SBPs were <100 , 100 to 119, 140 to 159, and ≥ 160 mm Hg, respectively. The highest and lowest SBP groups were associated with significantly increased risk of death ($P<0.05$) compared with the reference range.

The area under the receiver operating characteristic curve for the model with EFFECT-HF 1-year covariates was 0.718, increasing significantly to 0.722 on inclusion of discharge SBP in the model ($P=0.009$). Importantly, there was a substantial degree of reclassification to different blood pressure categories at discharge compared with those at the time of hospital admission. Among patients who had initial SBPs in the <100 , 100 to 119, 120 to 139, 140 to 159, and ≥ 160 mm Hg range, 63.6%, 56.1%, 66.5%, 80.2%, and 84.3% were reclassified to a different SBP category, respectively, at discharge. Similarly, among patients with an admis-

Table 1. Patient Characteristics by Categories of Discharge SBP

	SBP, mm Hg					P
	<100 (n=691)	100 to 119 (n=2350)	120 to 139 (n=2427)	140 to 159 (n=1379)	≥160 (n=601)	
Age, y, mean (SD)	73 (13)	75 (12)	75 (11)	76 (11)	76 (11)	<0.001
Male, n (%)	379 (54.8)	1269 (54.0)	1182 (48.7)	644 (46.7)	246 (40.9)	<0.001
Diabetes, n (%)	165 (23.9)	719 (30.6)	874 (36.0)	562 (40.8)	253 (42.1)	<0.001
Stroke or TIA, n (%)	97 (14.0)	344 (14.6)	396 (16.3)	237 (17.2)	111 (18.5)	0.048
Peripheral vascular disease, n (%)	81 (11.7)	270 (11.5)	295 (12.2)	196 (14.2)	88 (14.6)	0.06
COPD, n (%)	115 (16.6)	405 (17.2)	382 (15.7)	217 (15.7)	95 (15.8)	0.64
Prior myocardial infarction, n (%)	301 (43.6)	923 (39.3)	863 (35.6)	476 (34.5)	177 (29.5)	<0.001
Prior CABG, n (%)	84 (12.2)	293 (12.5)	268 (11.0)	147 (10.7)	55 (9.2)	0.13
Prior PCI, n (%)	28 (4.1)	67 (2.9)	77 (3.2)	34 (2.5)	14 (2.3)	0.25
Hemoglobin <10 g/dL or <100 g/L, n (%)	68 (9.8)	270 (11.5)	281 (11.6)	184 (13.3)	105 (17.5)	<0.001
Serum sodium <136 mmol/L, n (%)	179 (25.9)	478 (20.3)	487 (20.1)	254 (18.4)	128 (21.3)	0.002
Creatinine concentration, mg/dL, mean (SD)*	1.44 (0.92)	1.36 (0.77)	1.43 (1.08)	1.56 (1.24)	1.80 (1.46)	<0.001
LVEF <40%, n (%)	265 (38.4)	757 (32.2)	618 (25.5)	271 (19.7)	80 (13.3)	<0.001
ACE inhibitor or ARB, n (%)†	514 (74.4)	1639 (69.7)	1663 (68.5)	928 (67.3)	425 (70.7)	0.014
β-adrenoreceptor antagonist, n (%)†	201 (29.1)	633 (26.9)	665 (27.4)	379 (27.5)	176 (29.3)	0.7
Loop diuretic, n (%)†	556 (80.5)	1870 (79.6)	1915 (78.9)	1039 (75.3)	449 (74.7)	0.003

TIA indicates transient ischemic attack; COPD, chronic obstructive lung disease; CABG, coronary artery bypass graft surgery; PCI, percutaneous coronary intervention; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

*To convert creatinine to SI units ($\mu\text{mol/L}$), multiply by 88.4.

†Prescribed at discharge.

sion DBP <55, 55 to 64, 65 to 74, 75 to 84, or ≥ 85 , 74.7%, 61.9%, 64.7%, 80.3%, and 85.4% of patients were reclassified to another discharge DBP category, respectively.

Effect of Pulse Pressure

Median survival time ratios according to pulse pressure demonstrated similar, albeit attenuated, effects. Multivariable-adjusted survival time ratios were 0.90 (95% CI, 0.81 to 0.99), 0.96 (95% CI, 0.88 to 1.05), 1.00 (referent), 1.07 (95% CI, 0.96 to 1.20), and 0.97 (95% CI, 0.88 to 1.08) for pulse pressures <40, 40 to 49, 50 to 69, 70 to 79, and ≥ 80 mm Hg, respectively.

Life Expectancy

Estimated life expectancies based on discharge SBP and categories of the EFFECT-HF risk score are shown in Table 4. Within each risk group, a discharge SBP that was further removed from the middle range (120 to 139 mm Hg) was associated with decreased life expectancy. Reduced life expectancy at low and high discharge SBPs was observed in both men and women with reduced and preserved left ventricular systolic function.

Discussion

In current HF management, although guidelines do recommend angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and β -adrenoreceptor antagonists for therapy, there are few therapeutic considerations provided regarding blood pressure targets. For those with HF and preserved

LVEF, the effect of blood pressure on long-term survival has not been established. In this long-term analysis, we found that SBP at the time of hospital discharge was associated with death with a U-shaped pattern of risk, and similar patterns were observed for DBP. We found that the initial blood pressure at the time of acute HF presentation was only weakly associated with discharge blood pressure and that most patients were reclassified into different blood pressure strata at the time of discharge. Thus, admission and discharge blood pressures are distinct variables possibly reflecting different hemodynamic factors, with differing relationships to survival in patients with HF.

Among patients with coronary artery disease without HF, a J-shaped relationship was observed for DBP and the combined outcome of death or myocardial infarction.²³ In acute decompensated HF, previous studies have found that reduced (but not increased) SBP was strongly associated with mortality.²⁴ In the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure study, SBP >130 mm Hg did not predict postdischarge mortality at 60 to 90 days.¹⁰ The contrast may have been due, in part, to the longer duration of follow-up in our study, reflecting the long-term effects of increased blood pressure on ventricular hypertrophy or remodeling. In the Carvedilol Prospective Randomized Cumulative Survival study, lower baseline SBP was associated with higher mortality in patients with systolic HF, but measurements >125 mm Hg were grouped together, thus limiting the ability to examine a full range of blood pressures.¹¹ In the SOLVD [Studies of Left Ventricular

Table 2. Patient Characteristics by Categories of Discharge DBP

	DBP, mm Hg					<i>P</i>
	<55 (n=848)	55 to 64 (n=2173)	65 to 74 (n=2318)	75 to 84 (n=1432)	≥85 (n=677)	
Age, y, mean (SD)	78 (11)	76 (11)	75 (11)	74 (12)	72 (13)	<0.001
Male, n (%)	386 (45.5)	1084 (49.9)	1169 (50.4)	696 (48.6)	385 (56.9)	<0.001
Diabetes, n (%)	282 (33.3)	721 (33.2)	842 (36.3)	490 (34.2)	238 (35.2)	0.21
Stroke or TIA, n (%)	144 (17.0)	330 (15.2)	393 (17.0)	201 (14.0)	117 (17.3)	0.09
Peripheral vascular disease, n (%)	87 (10.3)	294 (13.5)	324 (14.0)	144 (10.1)	81 (12.0)	<0.001
COPD, n (%)	153 (18.0)	410 (18.9)	364 (15.7)	198 (13.8)	89 (13.1)	<0.001
Prior myocardial infarction, n (%)	332 (39.2)	836 (38.5)	897 (38.7)	468 (32.7)	207 (30.6)	<0.001
Prior CABG, n (%)	102 (12.0)	266 (12.2)	272 (11.7)	152 (10.6)	55 (8.1)	0.04
Prior PCI, n (%)	21 (2.5)	75 (3.5)	71 (3.1)	34 (2.4)	19 (2.8)	0.36
Hemoglobin <10 g/dL or <100 g/L, n (%)	132 (15.6)	321 (14.8)	250 (10.8)	150 (10.5)	55 (8.1)	<0.001
Serum sodium <136 mmol/L, n (%)	196 (23.1)	473 (21.8)	461 (19.9)	283 (19.8)	113 (16.7)	0.01
Creatinine concentration, mg/dL, mean (SD)*	1.49 (0.89)	1.44 (0.95)	1.44 (1.04)	1.46 (1.13)	1.58 (1.44)	0.02
LVEF <40%, n (%)	221 (26.1)	614 (28.3)	653 (28.2)	333 (23.3)	170 (25.1)	0.005
ACE inhibitor or ARB, n (%)†	604 (71.2)	1515 (69.7)	1582 (68.2)	989 (69.1)	479 (70.8)	0.471
[beta]-adrenoreceptor antagonist, n (%)†	224 (26.4)	577 (26.6)	682 (29.4)	398 (27.8)	173 (25.6)	0.131
Loop diuretic, n (%)†	680 (80.2)	1753 (80.7)	1787 (77.1)	1093 (76.3)	516 (76.2)	0.003

TIA indicates transient ischemic attack; COPD, chronic obstructive lung disease; CABG, coronary artery bypass graft surgery; PCI, percutaneous coronary intervention; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

*To convert creatinine to SI units ($\mu\text{mol/L}$), multiply by 88.4.

†Prescribed at discharge.

Dysfunction] trial, Domanski et al⁹ reported that a 10-mm Hg decrease in mean arterial pressure was associated linearly with an 11% increase in mortality risk. Our study extends the literature by demonstrating a U-shaped relationship between blood pressure and mortality, suggesting the hypothesis that an optimal range of blood pressures may exist in chronic HF with reduced or preserved left ventricular function.

Current guidelines do not recommend blood pressure “targets” specific to patients with HF. Our findings suggest that different blood pressure and hypertension management principles might potentially apply in patients with HF. In patients with acute HF, we¹ and others²⁴ found that SBP at initial hospital presentation is a potent predictor of early

mortality. The demonstration of a biphasic risk relationship at the upper and lower ranges of discharge blood pressure likely reflects the differing nature of acute and predischARGE chronic blood pressures in the patient with HF.

There are several potential mechanisms for a U-shaped relationship of blood pressure with mortality. Reduced SBP and DBP can affect cardiac events and performance by limiting coronary blood flow and may predispose to ischemic and arrhythmic events if chronic blood pressure is low.²⁵ Increased blood pressure may lead to cardiac remodeling and progression in atherosclerotic disease, which in turn may lead to subsequent ischemic events. Finally, both hypo- and hypertension may lead to noncardiac end-organ effects that result in the development of new or worsening comorbidities, including renal, cerebral, and peripheral vascular disease. Alterations in cardiac output may partly explain our observations because pulse pressure has been correlated with changes in cardiac output.²⁶ However, the effect of pulse pressure was attenuated, suggesting that other factors may be more important mechanisms for the U-shaped pattern of risk.

There are both clinical and research implications of our study. Blood pressure is a simple, cost effective, and potentially modifiable predictor of mortality, and therefore, it should be routinely followed. Clinically, our study does not suggest that HF medications of proven benefit should necessarily be withheld based on low blood pressure because their benefits are maintained irrespective of baseline blood pressure.²⁷ However, medications that lower blood pressure without a beneficial effect on prognosis could be reduced or

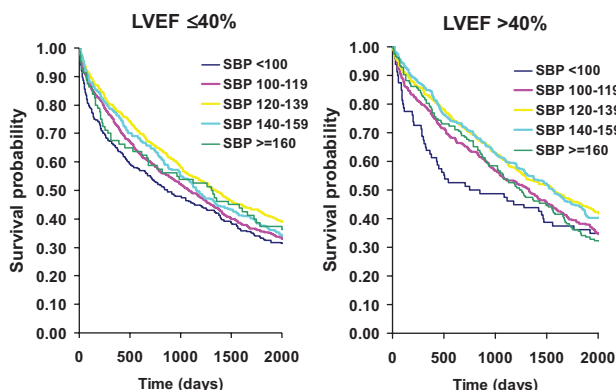


Figure 3. Kaplan–Meier survival curves by discharge SBP categories (overall log-rank $P<0.001$).

Table 3. Time-to-Event Analysis for Discharge Blood Pressure on Mortality Adjusted for EFFECT-HF Model and Medications at Discharge

	LVEF ≤40%		LVEF >40%		All HF	
	Median Survival Time Ratio	P	Median Survival Time Ratio	P	Median Survival Time Ratio	P
SBP						
<100	0.77 (0.62 to 0.97)	0.024	0.69 (0.51 to 0.93)	0.015	0.76 (0.67 to 0.85)	<0.001
100 to 119	0.83 (0.71 to 0.98)	0.029	0.83 (0.71 to 0.99)	0.034	0.90 (0.83 to 0.98)	0.015
120 to 139	1.00	Referent	1.00	Referent	1.00	Referent
140 to 159	0.75 (0.60 to 0.92)	0.007	0.95 (0.80 to 1.14)	0.58	1.00 (0.91 to 1.10)	0.98
≥160	0.75 (0.53 to 1.07)	0.12	0.76 (0.61 to 0.95)	0.016	0.90 (0.80 to 1.03)	0.12
DBP						
<55	0.81 (0.65 to 1.01)	0.07	0.76 (0.61 to 0.94)	0.011	0.83 (0.75 to 0.93)	<0.001
55 to 64	0.83 (0.71 to 0.98)	0.024	1.07 (0.90 to 1.26)	0.46	0.95 (0.87 to 1.03)	0.18
65 to 74	1.00	Referent	1.00	Referent	1.00	Referent
75 to 84	1.06 (0.86 to 1.30)	0.59	1.18 (0.98 to 1.42)	0.089	1.12 (1.02 to 1.23)	0.018
≥85	0.92 (0.70 to 1.20)	0.53	0.87 (0.67 to 1.14)	0.31	0.97 (0.86 to 1.10)	0.65

discontinued in patients with low blood pressure. In contrast, increased blood pressure before hospital discharge may indicate the need for additional antihypertensive therapy. Future research studies evaluating therapies for systolic or diastolic HF should also consider evaluation of therapeutic efficacy in those with low baseline blood pressure as an a priori hypothesis.

Our study had several notable limitations. Although discharge blood pressure was associated with death, determination of mechanisms and causality were beyond the scope of this study. However, the effects were significant despite controlling for multiple prognostic factors. Our determination of discharge blood pressure was made based on a single measurement in the prehospital discharge setting, and longi-

Table 4. Life Expectancy (in Years) Based on Discharge Blood Pressure Adjusted for EFFECT-HF Risk Score and Discharge Medications

SBP Category		Very Low Risk (≤60)	Low Risk (61 to 90)	Intermediate Risk (91 to 120)	High Risk (121 to 150)	Very High Risk (>150)
LVEF ≤40%						
Men	<100	10.29	5.02	2.18	1.04	0.47
	100 to 119	11.18	4.95	2.47	1.07	0.50
	120 to 139	13.36	6.18	2.93	1.30	0.63
	140 to 159	10.57	4.81	2.12	1.01	0.56
	≥160	11.27	5.43	2.16	1.01	0.37
Women	<100	9.38	4.65	2.16	1.01	0.43
	100 to 119	11.01	4.96	2.39	1.10	0.51
	120 to 139	12.51	6.03	2.89	1.30	0.65
	140 to 159	11.16	4.60	2.21	1.06	0.32
	≥160	10.83	5.12	2.07	0.84	0.54
LVEF >40%						
Men	<100	10.49	5.19	2.35	0.97	0.53
	100 to 119	11.74	5.52	3.00	1.30	0.73
	120 to 139	14.17	6.76	3.51	1.73	0.90
	140 to 159	11.00	6.96	3.42	1.68	0.82
	≥160	8.55	5.85	2.67	1.17	0.70
Women	<100	10.98	5.06	2.30	1.23	0.40
	100 to 119	12.86	5.70	2.84	1.33	0.57
	120 to 139	12.94	6.83	3.53	1.66	0.88
	140 to 159	11.73	6.44	3.39	1.74	0.62
	≥160	10.39	5.38	2.58	1.28	0.56

tudinal measurements may have varied. However, it is plausible that if such longitudinal variability was accounted for, an even greater effect on mortality would be anticipated. Our study did not examine doses of neurohormonal antagonists in patients who had lower blood pressure nor did we determine whether achieving different blood pressure targets in hypertensive patients would reduce intermediate cardiac events in addition to mortality. Finally, although our analyses adjusted extensively for important covariates, there remains the potential for residual confounding and the possibility that discharge blood pressure may be a marker of HF severity rather than a target for therapy. Despite the above-mentioned limitations, our results draw attention to the need for further study of this important parameter as a potential mechanism to improve outcomes and determine therapeutic adequacy, and as a simple marker of mortality risk in stable HF in a randomized controlled trial.

In conclusion, discharge blood pressure is associated with mortality in a U-shaped pattern of risk in patients with HF. The transition phase from acute to chronic HF at the time of hospital discharge represents a window of opportunity to identify patients with blood pressures that reside in a high-risk range. Patients with low discharge blood pressure may need more frequent clinical assessment and blood pressure monitoring, whereas those with high discharge blood pressure may benefit from additional antihypertensive medications to reduce their risk.

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Disclosures

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CLINICAL PERSPECTIVE

Higher blood pressure in acute heart failure has been associated with improved survival; however, the relationship between blood pressure and survival in stabilized patients at hospital discharge has not been established. We examined the long-term survival impact of systolic and diastolic blood pressure measured before discharge from the hospital in 7448 patient with heart failure. The blood pressure at the time of acute hospital presentation and the discharge blood pressure differed substantially. We found a U-shaped pattern of mortality risk with discharge blood pressure. In those with LVEF $\leq 40\%$, median survival decreased by 17%, 23%, and 25% when discharge systolic blood pressure was <100 , 110 to 119, and ≥ 140 mm Hg, respectively, compared with those in the midrange (120 to 139 mm Hg) after multivariable adjustment. In those with LVEF $>40\%$, adjusted median survival decreased by 31%, 17%, and 24% when discharge systolic blood pressures were <100 , 100 to 119, and ≥ 160 mm Hg, respectively, compared with those in the 120 to 139 mm Hg range. In patients with heart failure, discharge blood pressure is associated with mortality in a U-shaped pattern of risk. The transition phase from acute to chronic heart failure at the time of hospital discharge represents a window of opportunity to identify patients with blood pressures that reside in a high-risk range. Patients with low discharge blood pressure may need more frequent assessments and blood pressure monitoring, whereas those with high discharge blood pressure may benefit from additional antihypertensive medications.