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Elevation in systolic blood pressure during heart failure hospitalization is associated with increased short and long-term mortality

Omer Segal, BMedSc[a,*], Gad Segal, MD[b], Avshalom Leibowitz, MD[a,c], Ilan Goldenberg, MD[a,c,d], Ehud Grossman, MD[a,e], Robert Klempfner, MD[a,f]

Abstract

The relationship between systolic blood pressure (SBP) change during hospitalization of patients with heart failure (HF) and clinical outcomes has never been thoroughly investigated.

A total of 3393 patients hospitalized with HF, from 25 hospitals in Israel, were enrolled. The SBP change was calculated by subtracting the discharge SBP values from the admission values and then divided into quartiles of SBP change. We compared the group with upper quartile SBP change to the lower 3 quartiles of change. Both groups had largely similar demographics and clinical characteristics. All-cause mortality rate was 24% at 1-year and 82.6% at 10-years, whereas patients in the upper SBP change group had significantly higher cumulative mortality probability at 1-year (30% vs 22%; log-rank $P<0.001$), and at 10-years (86% vs 82%; log-rank $P<0.001$). Multivariate Cox proportional hazard analysis adjusted for comorbidities demonstrated that patients in the upper SBP change quartile have an independent 17% higher mortality risk at 10-years [hazard ratio (HR) 1.17; 95% confidence interval (CI) 1.08–1.28]. Subgroup analysis demonstrated that mortality risk was more pronounced in patients with preserved ejection fraction and in the subgroup with admission SBP ≥140 mm Hg.

SBP change is significantly associated with 1- and 10-year all-cause mortality, as an increased SBP change is associated with worse prognosis. We believe that this readily available marker might facilitate risk stratification of patients and possibly improve care.

Abbreviations: ACE-I = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, CI = confidence interval, eGFR = estimated glomerular filtration rate, HF = heart failure, HFpSF = heart failure with preserved systolic function, HFrSF = heart failure with reduced systolic function, HFSIS = heart failure survey in Israel, HR = hazard ratio, LVEF = left ventricular ejection fraction, MI = myocardial infarction, MRA = mineralocorticoid receptor antagonists, NYHA = New York Heart Association, SBP = systolic blood pressure.

Keywords: heart failure, mortality, prognosis, systolic blood pressure

1. Introduction

Heart failure (HF) is a common cause for hospitalizations, especially in the elderly population.[1] It is well established that patients with HF diagnosis are at high risk for mortality and rehospitalization in the early period after discharge,[2,3] thus becoming a major burden on health care services around the world. Accordingly, identification of risk factors for short and long outcomes in hospitalized HF patients is important for appropriate risk stratification and management of this population.

While it was well established that low baseline systolic blood pressure (SBP) at admission is associated with increased in-hospital mortality[4,5] and mortality in up to 5-years after hospitalization,[3,4,6,7] the association between the SBP change from admission to discharge and subsequent outcome has never been thoroughly investigated.

The present study was carried out among 3393 patients enrolled in the Heart Failure Survey in Israel (HFSIS) and was designed to investigate the association between SBP change and all-cause mortality at 1- and 10-years posthospitalization follow-up.

2. Methods

2.1. Study population and protocol

This multicenter national survey was conducted in 25 hospitals in Israel between March and April 2003. It is comprised from 93 of 98 internal medicine and 24 of 25 cardiology departments operating in Israel at the time. Its design and methods were described in detail in previous reports.[8–10]

Heart failure was established on the basis of subjective symptoms of HF, such as fatigue and dyspnea at rest or exercise

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[a] Sackler Faculty of Medicine, Tel Aviv University, Tel-Aviv, [b] Internal Medicine "T", Chaim Sheba Medical Center, Tel Hashomer, [c] Leviev Heart Center, Sheba Medical Center, Tel HaShomer, Ramat Gan, Israel, [d] Heart Research Follow-Up Program, University of Rochester Medical Center, Rochester, NY, [e] Internal Medicine D and Hypertension Unit, The Chaim Sheba Medical Center, Tel-Hashomer, [f] Cardiac Rehabilitation Institute, Chaim Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel.

[*] Correspondence: Omer Segal, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel (e-mail: omersgl@gmail.com).

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and objective findings on physical examination made by qualified physicians (edema, pulmonary edema, jugular veins distention). Evidence of cardiac dysfunction at rest was made by noninvasive tests such as chest radiography, echocardiography, cardiac scintigraphy, or ventriculography. Acute HF was defined as a rapid change in signs and symptoms that necessitated urgent medical care (cardiogenic shock, mechanical support, etc.) and was categorized as either acute de novo HF or acute exacerbation of previously diagnosed HF. The following information was collected and abstracted by physicians in the participating departments: demographics, medical history and chronic medication, physical examination findings, laboratory data, New York Heart Association (NYHA) functional classification prior to the acute event, HF etiology and suspected precipitating factors of current event, electrocardiogram, chest radiography, in-hospital management and events and hospitalization outcome. The protocol of this study was approved by the ethics committee at each of the participating hospitals and was managed in accordance with the Declaration of Helsinki. Informed consent was obtained by the patients or by their guardians and all the data was documented and analyzed anonymously on designated electronic files.

The HFSIS survey included patients who met the aforementioned diagnosis criteria of HF. We excluded patients who died during hospitalization (n = 193), patients lacking admission and predischarge blood pressure measurements (n = 290), patients with admission systolic values below 90 mm Hg (n = 226), patients with initial diagnosis of HF later refuted by additional findings, admission to cardiac surgery departments, subjects participating refusal and missing crucial data. Thus, a total of 3393 patients were included in the present analysis.

2.2. Blood pressure evaluation

The arrival SBP was the first measurement following the arrival to the emergency room, and the discharge SBP was the last measurement prior to discharge. These values were prospectively defined and collected by research personal.

Blood pressure was measured by a medical device grade sphygmomanometer available in emergency department and other medical care units. Health care personal were instructed to follow the recommended blood pressure measurement techniques: 2 consecutive measurements, 1 to 3 minutes apart. The second measurement was recorded. With the exception of admission SBP, which was measured at first contact with medical personnel, the following blood pressure measurement was made at fixed time of the day, which was not stated at the HFSIS database. Blood pressure was measured 3 times a day at the beginning of each nursing shift (07:00, 15:00, 23:00). Where the clinical condition indicated and in intensive care environments, measurements were made every 1–3 hours or continuously by arterial catheterization.

2.3. Definitions and outcome measures

Prespecified study endpoints were: 1-year and 10-year all-cause mortality outcomes. In-hospital mortality and adverse event were collected from registry forms and vital status confirmed from the National Population Registry in Israel.

Signs and symptoms (at least 1 of each) had to be present in order to diagnose HF. additionally, in the vast majority of cases HF diagnosis was further supported by noninvasive testing as mentioned above. A working diagnosis of HF was made on admission based on the constellation of clinical findings and noninvasive testing (online supplemental Table 3, http://links.lww.com/MD/B530). The clinical diagnosis of both heart failure with preserved systolic fraction (HFpSF) and heart failure with reduced systolic fraction (HFrSF) was further validated by senior staff member.

Hypertension was defined as SBP ≥140 mm Hg, DBP ≥ 90 mm Hg, or antihypertensive therapy. Diabetes was defined as fasting plasma glucose level >7.8 mmol/L, a glucose level >11.1 mmol/L 2 hours after glucose challenge test, or chronic treatment for diabetes. Other comorbidities were defined as previously published before.[11]

As blood pressure change is significantly influenced by the admission blood pressure, and low admission SBP is a well-established predictor of poor outcomes, we undertook a subgroup analysis where the effect of SBP change was explored in patients with SBP admission values ≥140 mm Hg only.

2.4. Statistical analysis

Variables are expressed as mean ± standard deviation, and categorical data is summarized as frequencies and percentages. Blood pressure change was calculated by subtracting the discharge value from the admission value, thus positive values represent a BP increase during hospitalization and higher blood pressure values at discharge. The obtained results (BP difference) were further separated into quartiles. We compared the high SBP change group (upper quartile of SBP change) to the lower SBP change groups (the 3 lower quartiles of SBP change). Comparison of categorical variables was performed with χ^2 analysis and comparison of continuous variables was performed with the Student t test for variables with normal distribution and by Kruskal–Wallis for those that violated the normality assumption.

Logistic regression modeling was employed in order to identify independent predictors of greater SBP change (upper quartile SBP group). Covariates that were highly significant in a univariate model were introduced in a multivariate model using the best subset method: age, gender, New York Heart Association (NYHA) class >II, anemia (defined as hemoglobin <11 g/dL), admission SBP as a continuous variable, estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 using the MDRD formula, HFpSF (vs HFrSF), and admission heart rate as a continuous variable.

The Kaplan–Meier method was used to determine cumulative probabilities of death from any cause from the time of admission throughout the follow-up period, according to BP change quartile, with between-group comparisons of cumulative event rates compared by means of the log-rank test. Curves were generated separately for the 1-year and 10-year all-cause mortality outcomes. Additional analysis was similarly performed comparing outcomes of patients in the upper quartile of BP change to lower quartiles in subgroups of patients with admission SBP value ≥140 mm Hg.

In order to evaluate the independent association of SBP increase and all-cause mortality, we undertook multivariate Cox proportional-hazards regression analyses. The Cox model was adjusted for relevant prespecified clinical covariates with the use of best-subset regression modeling. The following covariates were introduced in addition to upper quartile SBP change (compared with the lower 3 quartiles): age, serum creatinine level, presence or absence of diabetes mellitus, NYHA functional class, hyponatremia (first available serum sodium <135 mmol/L), past myocardial infarction (MI), chronic obstructive pulmonary disease, admission systolic blood pressure, precipitating factors

(ischemic, infectious, nonadherence to therapy), and in-hospital modifications of major therapeutic drug classes (diuretics, angiotensin receptor blockers or angiotensin converting enzyme inhibitors, beta blockers, MRA, calcium channel blockers, and alpha blockers). Additionally, the above-described analysis was repeated including only patients with admission SBP ≥140 mm Hg. We similarly undertook an analysis where SBP change was evaluated as percent change from baseline (admission values subtracted from the discharge values and then divided by the admission values) and was introduced in the described models as a continuous variable.

In order to evaluate the risk associated with each SBP change quartile, we compared each quartile against the lowest SBP change quartile, serving as the reference value, in a model adjusted for age, gender, eGFR (dichotomized at <60 mL/min/1.73 m^2), left ventricular ejection fraction (LVEF) (as continuous variable), and NYHA functional class. We repeated this multivariate analysis without a reference group and introduced each quartile group (Q1 to Q4) separately to explore the independent associated risk with each separate group. In addition, we separately analyzed the subgroup of subjects with HFpSF and HFrSF and explored mortality risk associated with the upper SBP change quartile (vs lower quartiles) in each subgroup. Cox regression model proportionality of hazard assumption verification by Schoenfeld residuals and the log minus log method (LML).

Finally, we performed interaction term analysis, using the entire population, in order to explore the effect of upper quartile SBP change group in subgroups of patients with admission SBP ≥140 versus <140 mm Hg. The regression model was adjusted for age, gender, eGFR (dichotomized at <60 mL/min/1.73 m^2), LVEF (as a continuous variable), and NYHA functional class. *P* values for interactions are reported.

All *P* values were 2 sided, and a *P* value ≤0.05 was considered significant. The statistical software used was SPSS version 20 (IBM Inc, New York).

3. Results

3.1. Admission and discharge characteristics by SBP change group

The HFSIS survey comprised 4102 patients, 3393 (83%) of whom met this study's inclusion criteria. The cohort comprised mostly of male patients (57%), 73 ± 12 years old, 38% with NYHA class III or IV symptoms, 61% with prior HF hospitalizations, and 19% with preserved systolic function. As described, we divided SBP change into quartiles according to the degree of SBP change (discharge value minus admission value). The following blood pressure change ranges were obtained: Q1 ≤−29 mm Hg; Q2 = −28 to −10 mm Hg; Q3 = −9 to 3 mm Hg, and Q4 ≥ 4 mm Hg (Fig. 1—online supplemental content, http://links.lww.com/MD/B530). The upper quartile (Q4) represents the group that increased their SBP to the greatest extent.

Comparison of patients' characteristics was performed between the upper quartile of SBP change (upper SBP change group) and the 3 lower quartiles. Past medical history, demographics, and comorbidities were largely similar, whereas duration of HF hospitalizations was shorter in the upper quartile group (Q4 5.3 ± 4.4 days vs lower 3 quartiles 5.7 ± 6.1 days; $P < 0.01$). Significant differences were evident mainly in the admission vital signs, preadmission medications, and laboratory results (Table 1).

Compared with patients in the 3 lower SBP change quartiles, patients in the upper quartile of SBP change had lower heart rate, lower admission systolic blood pressure, and were more likely to have diabetes, NYHA functional class III–IV and receive furosemide chronically prior to admission. Furthermore, patients in the upper SBP change quartile were discharged with higher SBP and heart rate, and were more likely to receive amiodarone prescription. Blood pressure lowering medications prescribed at discharge did not differ significantly between the groups (Table 2). Additionally, the percent of medication changes (discharge drug class rate vs admission rate) did not differ significantly between Q4 versus Q1–3 group, with the exception of angiotensin converting enzyme inhibitor/angiotensin receptor blocker (ACE-I/ARB) rates that were decreased in the Q4 group (−7%) and increased in the Q1–3 group (+4%; $P = 0.01$; Table 1—online supplemental content, http://links.lww.com/MD/B530).

3.2. Predictors of upper SBP change quartile

We identified a number of independent predictors of greater SBP change (patients in the upper quartile of SBP change) including significant anemia (defined as hemoglobin <11 g/dL) and having a diagnosis of HFpSF. Conversely, higher admission systolic blood pressure and heart rate were independently associated with lower likelihood of having great SBP change in the upper quartile group (Table 2—online supplemental content, http://links.lww.com/MD/B530).

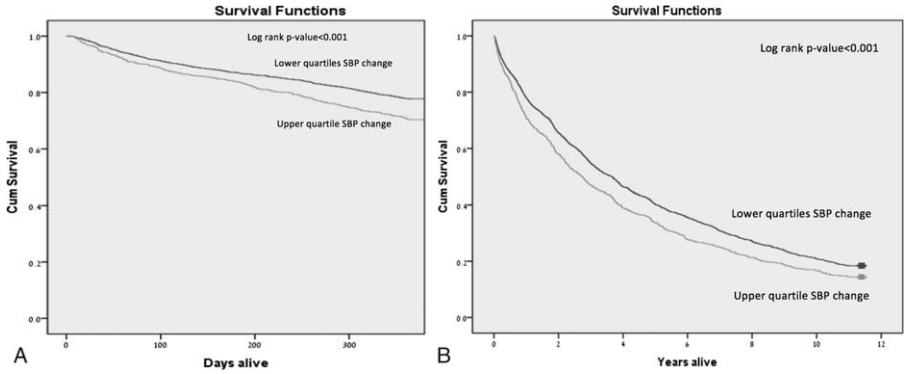

Figure 1. Kaplan–Meier curves. A, Kaplan–Meier estimates for 1-year all-cause mortality for patients in the upper SBP change quartile versus patients in the 3 lower SBP change quartiles (log-rank *P* value <0.001). B, Kaplan–Meier estimates for 10-year all-cause mortality for patients in the upper SBP change quartile versus patients in the 3 lower SBP change quartiles (log-rank *P* value <0.001). SBP = systolic blood pressure.

Table 1

Baseline admission characteristics of 3393 hospitalized patients with heart failure by change in systolic blood pressure.

Admission characteristics	Upper quartile (n = 838)	Lower quartiles (n = 2555)	*P* value
Age, y	73 ± 13	73 ± 12	0.95
Female, n (%)	354 (42)	1091 (43)	0.82
BMI, median (IQR)	26.8 (24.2–30.6)	26.2 (23.8–29.8)	0.05
Smoking, n (%)	262 (31)	731 (29)	0.10
Previous HF Hospitalizations, n (%)			0.83
N = 0	233 (30)	831 (35)	
N = 1–2	321 (42)	946 (41)	
N ≥3	212 (28)	580 (25)	
Vital signs, median (IQR)			
Heart rate, bpm	80 (68–92)	82 (70–98)	<0.001
SBP, mm Hg	120 (108–135)	150 (130–170)	<0.001
SBP <140 mm Hg	682 (81)	1044 (41)	<0.001
DBP, mm Hg	69 (60–77)	80 (70–90)	<0.001
Sinus rhythm, n (%)	589 (70)	1855 (73)	0.28
Left ventricular systolic dysfunction, n (%)			0.23
Preserved (LVEF ≥50%)	152 (27)	491 (28)	
Mild (40%≤LVEF≤49%)	113 (20)	414 (23)	
Moderate (30%≤LVEF≤39%)	457 (26)		
151 (27)			
Severe (LVEF≤29%)	154 (27)	424 (24)	
NYHA class, n (%)	0.02		
I	155 (19)	500 (20)	
II	325 (40)	1035 (42)	
III	258 (32)	787 (31)	
IV	82 (9)	168 (7)	
Medical history, n (%)			
Diabetes	381 (46)	1058 (41)	0.04
Hypertension	564 (67)	1803 (71)	0.07
Dyslipidemia	315 (38)	928 (36)	0.53
Past-MI	337 (40)	978 (38)	0.32
Post-CABG	134 (16)	395 (15.5)	0.72
Post-PCI	124 (15)	407 (16)	0.40
CAD	594 (71)	1806 (71)	0.93
Jugular V. distention	228 (27)	758 (30)	0.20
S/P stroke	114 (14)	319 (13)	0.42
PVD	86 (10)	224 (9)	0.23
COPD	172 (21)	503 (20)	0.62
Medications prior to admission, n (%)			
MRA	122 (15)	349 (14)	0.48
ACE-I\ARB	609 (74)	1724 (66)	0.16
Statins	304 (36)	913 (36)	0.73
β-Blocker	420 (50)	1262 (49)	0.62
Furosemide	542 (65)	1526 (59)	0.007
Ca. blockers	226 (27)	689 (27)	0.93
Nitrates	288 (34)	905 (35)	0.65
Aspirin	511 (61)	1509 (59)	0.25
Digoxin	104 (12)	343 (13)	0.48
Amiodarone	103 (12)	229 (9)	0.004
Laboratory values			
Anemia (Hb <11 g/dL), n (%)	274 (33)	659 (26)	<0.001
eGFR <60 mL/min/1.73 m^2	463 (57)	1355 (54)	0.21
Urea (mg/dL), median (IQR)	48 (32–75)	45 (30–67)	0.002
Glucose (mg/dL), median (IQR)	133 (103–198)	132 (105–187)	0.81
Na (mEq/L), median (IQR)	138 (135–141)	139 (136–141)	0.001
Total chol (mg/dL), median (IQR)	163 (137–196)	175 (146–205)	<0.001
K (mEq/L), median (IQR)	4.4 (4–4.8)	4.3 (3.9–4.7)	0.03

Quantitative data is presented as mean ± standard deviation and median (IQR), and qualitative data as absolute frequencies and percentages.

P values are for the difference between the upper quartile and the 3 lower quartiles.

ACE-I = angiotensin converting enzyme inhibitor, ARB angiotensin receptor blocker, BMI = body mass index, bpm = beats per minute, CABG = coronary artery bypass graft, CAD = coronary artery disease, Chol = cholesterol, COPD = chronic obstructive pulmonary disease, DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, MI = myocardial infarction, MRA = mineralocorticoid antagonists, NYHA = New York Heart Association, PCI = percutaneous coronary intervention, PVD = peripheral vascular disease, SBP = systolic blood pressure.

Table 2

Discharge characteristics of 3393 hospitalized patients with heart failure by change in systolic blood pressure.

Characteristics	Upper quartile (n = 838)	Lower quartiles (n = 2555)	*P* value
Vital signs, median (IQR)			
Heart rate, bpm	74 (65–81)	72 (64–80)	0.005
SBP, mm Hg	140 (124–156)	128 (114–140)	<0.001
DBP, mm Hg	74 (67–80)	70 (61–80)	<0.001
Discharge medications, n (%)			
ACE-I or ARB	560 (67)	1788 (70)	0.13
MRA	164 (20)	530 (21)	0.52
Statins	333 (40)	1085 (42)	0.23
Furosemide	620 (74)	1901 (74)	0.99
β-Blocker	482 (58)	1570 (61)	0.07
Aspirin	555 (66)	1777 (69)	0.11
Anticoagulants	184 (22)	486 (19)	0.06
Digoxin	111 (13)	371 (14)	0.42
Nitrates	287 (34)	934 (36)	0.27
Ca blockers	219 (26)	683 (27)	0.86
Amiodarone	114 (14)	260 (10)	0.005

3.3. Survival by SBP change quartiles in the entire study population

All-cause mortality of the entire cohort was 24% at 1-year and 82.6% at 10 years of follow-up. Patients in the upper SBP change quartile had significantly higher mortality compared with those in the lower quartiles, at 1-year (30% vs 22%; log-rank *P* value < 0.001; Fig. 1A), and at 10-years (86% vs 82%; log-rank *P* value <0.001; Fig. 1B).

Consistently, multivariate analysis demonstrated that patients in the upper SBP change quartile experienced a significant 17% higher mortality risk at 10-years of follow-up [hazard ratio (HR) 1.17; confidence interval (CI) 1.08–1.28]. Additional covariates significantly associated with long-term mortality included: hyponatremia, eGFR below 60 mL/min/1.73m^2, NYHA functional class III–IV, diabetes, and history of a prior MI (Table 3). A graded relationship between SBP change quartile and mortality is presented in Fig. 2.

Furthermore, consistent results were obtained when SBP change was evaluated as a continuous variable, each 1% increase from baseline values was associated with an adjusted mortality risk increment of 1.3% ($P < 0.001$).

Additionally, we explored the independent risk associated with each SBP change quartile (Q1 to Q4). The low SBP change quartile (Q1) was associated with lower mortality risk (HR 0.88; CI 0.81–0.96), whereas the upper quartile (Q4) was associated with the highest mortality risk (HR 1.22; CI 1.12-1.33) (online supplemental data, http://links.lww.com/MD/B530, Fig. 3).

Finally, we compared the HFpSF group to the HFrSF group. The upper quartile SBP change was similarly associated with greater mortality risk, more pronounced in the HFpSF group (HR 1.25; 1.01–1.54 and HR 1.18; CI 1.07–1.30, respectively). Precipitating factors rates for HF hospitalization were relatively similar between the 2 groups and are summarized in Table 3—online supplemental data, http://links.lww.com/MD/B530.

Table 3

Independent predictors of long-term all-cause mortality of the entire study population and of patients with admission systolic blood pressure ≥140 mm Hg.

	The entire HFSIS population (SBP>90 mm Hg)				Admission SBP≥140 mm Hg			
		95% CI				95% CI		
	HR	Lower	Upper	*P* value	HR	Lower	Upper	*P* value
Upper quartile SBP change	1.17	1.08	1.28	<0.001	1.21	1.02	1.43	0.027
Admission SBP ≥ 140 mm Hg	0.88	0.81	0.96	0.004	—	—	—	—
Age (per year increment)	1.04	1.04	1.05	<0.001	1.04	1.04	1.05	<0.001
NYHA class >2	1.32	1.26	1.39	<0.001	1.25	1.17	1.34	<0.001
eGFR <60 mL/min/1.73 m^2	1.41	1.29	1.53	<0.001	1.32	1.18	1.48	<0.001
Sodium <135 mmol/L	1.34	1.13	1.58	0.001	1.18	0.92	1.52	0.19
Anemia (hemoglobin <11)	1.25	1.15	1.36	<0.001	1.28	1.14	1.44	<0.001
Past MI	1.11	1.02	1.20	0.012	1.07	0.96	1.19	0.24
Diabetes mellitus	1.23	1.14	1.33	<0.001	1.18	1.06	1.32	0.002
COPD	1.32	1.20	1.45	<0.001	1.21	1.06	1.37	0.004

CI = confidence interval, HR = hazard ratio.

Including precipitating factors in the Cox analysis did not significantly alter the results.

3.4. Prognosis of patients with admission SBP ≥140 mm Hg and <140 mm Hg by quartiles of SBP change quartile

In order to explore whether the impact on mortality is driven by patients with relatively low admission SBP, where larger increase in SBP simply represent a more fragile subgroup, we examined the subgroup with SBP ≥140 mm Hg (140 mm Hg representing the entire cohort admission median value) comprising 1842 (54%) patients.

In this subgroup separately analyzed, similar to the entire population, unadjusted long-term mortality rates of patients in the upper SBP change quartile were significantly higher than the rates in the lower SBP change quartiles (90% vs 84%, respectively; log-rank *P* value = 0.006; Fig. 3B). Similar mortality rates were noted in the subgroup of patients with admission SBP <140 mm Hg (Fig. 3A). Consistently, multivariate analysis in this subgroup demonstrated 21% greater adjusted mortality risk in subjects of the SBP upper quartile group (HR 1.21; CI 1.02–1.43; Table 3).

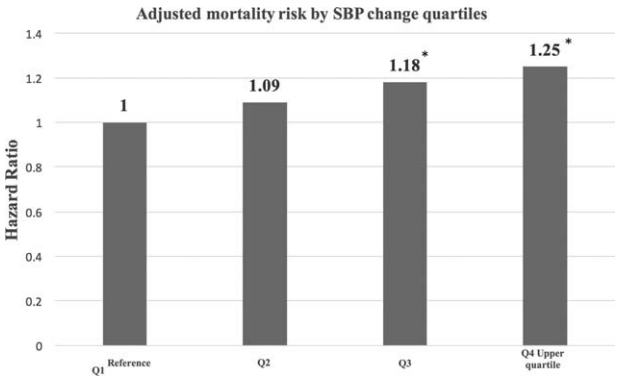

Figure 2. Adjusted all-cause mortality risk by SBP change quartile demonstrating a graded relationship between SBP change quartile and mortality in the entire study population (*P* value <0.05 compared with Q1 serving as the reference value; *P* value for trend <0.01; model adjusted to age, gender, eGFR, LVEF, and NYHA functional class). eGFR = estimated glomerular filtration rate, LVEF = left ventricular ejection fraction, NYHA = New York Heart Association, SBP = systolic blood pressure.

Subgroup analysis by interaction term modeling using the entire study cohort consistently demonstrated a significant 22% greater mortality risk associated with the upper quartile of SBP change in the patient group with admission SBP ≥ 140 (HR 1.22; CI 1.08–1.38; *P* = 0.002; Fig. 2—online supplemental content, http://links.lww.com/MD/B530), whereas SBP change quartile was not associated with a statistically significant mortality risk in the subgroup of patients with admission SBP <140 mm Hg (HR 1.01; 95% CI 0.88–1.70; *P* = 0.87; Fig. 2—online supplemental content, http://links.lww.com/MD/B530). Consistent results were obtained when we compared patients with admission SBP ≥120 mm Hg to those with SBP <120 mm Hg.

4. Discussion

To our knowledge, the present study is the first to assess the association between blood pressure change during hospitalization for HF and subsequent prognosis following discharge. We have shown that in a large population of heart failure patients comprising both HFpSF and HFrSF patients, systolic blood pressure change from admission to discharge is associated with an important effect on short- and long-term survival. The upper quartile SBP change group values were associated with reduced survival rates, a finding that persists following multivariate analysis. These findings were consistent when patients with HFpSF were separately evaluated. Furthermore, long-term mortality risk increased linearly when SBP change was introduced a continuous variable or when upper quartiles were compared to the low SBP change quartile. Furthermore, our findings suggest that SBP increase during hospitalization provides incremental prognostic information among patients with higher baseline SBP values on admission (≥140 mm Hg), whereas the risk associated with BP change during hospitalization appears to be attenuated among those with lower baseline SBP values.

The prognostic significance of admission SBP has been thoroughly described. Low admission SBP is associated with clinical worsening and mortality during hospitalization of patients with HF,[12–14] even in patients with preserved LVEF.[5] Moreover, patients with lower admission SBP are more likely to be referred to hospice after hospitalization with HF,[15] while elevated baseline SBP on admission correlates significantly with decreased in hospital all-cause mortality.[16] Low admission SBP was also associated with 5-year all-cause mortality in patients with preserved EF.[17] Nunez et al[18] demonstrated that in

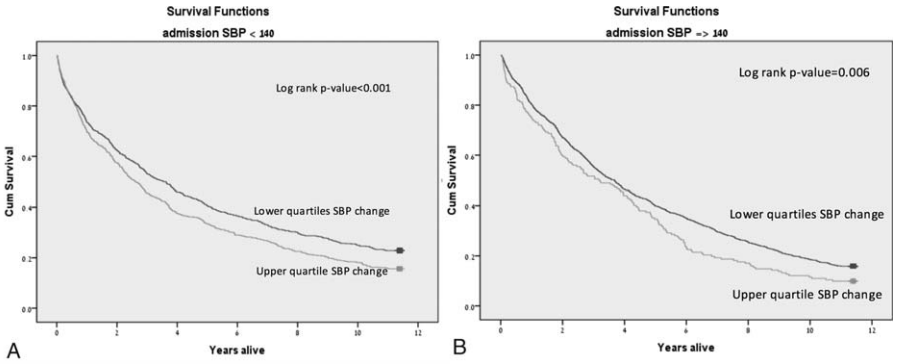

Figure 3. Kaplan–Meier curves. A, Kaplan–Meier estimates for 10-year all-cause mortality for patients in the upper SBP change quartiles versus patients in the 3 lower SBP change quartiles in the subgroup of patients with admission SBP lower than 140 mm Hg (log rank *P* value <0.001). B, Kaplan–Meier estimates for 10-year all-cause mortality for patients in the upper SBP change quartiles versus patients in the 3 lower SBP change quartiles in the subgroup of patients with admission SBP equal to or higher than 140 mm Hg (log rank *P* value = 0.006). SBP = systolic blood pressure.

patients with LVEF≤40%, admission SBP is linearly and inversely associated with mortality, while patients with LVEF ≥ 50% showed a J-shape pattern in this study, with a median follow-up of 18 month postdischarge.

Low SBP at discharge was also found to have substantial association with prognosis, as it is associated with increased all-cause mortality, cardiovascular mortality, and rehospitalization of patients with HF.[19] Nevertheless, lower SBP, measured 2 weeks after hospitalization with acute HF, was found to be associated with fewer adverse clinical outcomes.[20] Yet, this study was conducted on a small cohort and these findings should be validated on larger population.

To the best of our knowledge, Svensson et al[21] were the only ones who tried to describe the association between SBP change and mortality in a group of 208 HF patients. A univariate analysis demonstrated that SBP reduction during hospitalization is associated with 1-year all-cause mortality. Yet, this finding was not statistically significant when multivariate analysis was employed.

The importance of blood pressure and its impact on outcomes is well recognized; therefore, patterns of behavior of SBP during hospitalization can possibly serve as a readily available marker of increased short and long-term mortality. We can only speculate on the mechanism responsible for the observed reduced survival of subjects in the high SBP change quartile group. It is possible that patients experiencing greater change received less medication titration during their hospital stay or represent a subgroup with greater degree of neuro-hormonal activation that is well correlated with outcomes.[22–24] Indeed, patients in the upper quartile had a higher discharge heart rate.

Another possibility we need to consider is that patients who experienced SBP pressure increase represent a subgroup of patients with higher baseline values that present with lower values on admission and gradually increase their SBP values over the course of their hospital stay. We have no preadmission data to verify this hypothesis.

The SPRINT study results, which demonstrated that when patients with SBP higher than 130 mm Hg or an increased cardiovascular risk received an intensive treatment to a target goal of SBP <120, the mortality and cardiovascular complications rate was lower, compared with the standard treatment group whose goal was set as SBP <140 mm Hg.[25] In light of those findings, we can speculate that greater SBP values, which we currently consider normal, might have long-term implications on patients' prognosis, and SBP elevation during hospitalizations should be carefully examined. Further prospective studies are needed to support this assumption.

5. Limitations

Our study has a number of important limitations. The study is based on multicenter prospective national registry, yet not all possible confounders can be adjusted for. The HFSIS registry has no data regarding postdischarge treatment or clinical events other than all-cause mortality. Also, we do not have detailed information regarding in-hospital medication doses and cannot adjust for dose changes. We could only include adjustment for medication changes on admission and discharge. The main outcome was defined as all-cause mortality, as data regarding the cause of death, including cardiovascular mortality or adverse events, was not available. Finally, the exact time of blood pressure measurements was not recorded in the HFSIS registry and therefore could not be adjusted for.

6. Conclusions

Systolic blood pressure change during hospitalization for heart failure has prognostic significance, greater changes being associated with increased short and long-term mortality, especially among patients with higher baseline SBP values. Evaluating this change can facilitate risk stratification and possibly improve care. These findings need to be further validated in additional heart failure populations.

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