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Associations of short- and long-term mortality with admission blood pressure in Chinese patients with different heart failure subtypes

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Abstract

It remains unknown whether systolic (SBP) and diastolic (DBP) pressure on admission are associated with short- and long-term mortality in Chinese patients with heart failure with preserved (HFpEF), mildly reduced (HFmrEF), and reduced (HFrEF) ejection fraction. In 2706 HF patients (39.1% women; mean age, 68.8 years), we assessed the risk of 30-day, 1-year, and long-term (> 1 year) mortality with 1-SD increment in SBP and DBP, using multivariable logistic and Cox regression, respectively. During a median follow-up of 4.1 years, 1341 patients died. The 30-day, 1-year, and long-term mortality were 3.5%, 16.7%, and 39.4%, respectively. In multivariable-adjusted analyses additionally accounted for DBP or SBP, a higher SBP conferred a higher risk of long-term mortality (hazard ratio, 1.11; 95% CI, 1.02-1.22; $p = .017$) and a lower DBP was associated with a higher risk of all types of mortality ($p \leq .011$) in all HF patients. Independent of potential confounders including DBP or SBP, in patients with HFpEF, higher SBP and lower DBP levels predicted a higher risk of long-term mortality with hazard ratios amounting to 1.16 (95% CI, 1.04–1.29; $p = .007$) and .89 (95% CI, .80–.99; $p = .028$), respectively. In patients with HFmrEF and HFrEF, irrespective of adjustments of potential confounders, DBP was associated with 1-year mortality with odds ratios ranging from .49 to .62 ($p \leq .006$). In conclusion, lower DBP and higher SBP levels on admission

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were associated with a higher risk of different types of all-cause mortality in Chinese patients with different HF subtypes. Our observations highlight that admission BP may help to improve risk stratification.

KEYWORDS
blood pressure, ejection fraction, heart failure, mortality

1 | INTRODUCTION

Heart failure (HF) is a major public health concern affecting at least 26 million people worldwide and causing a tremendous economic burden.[1] The prevalence of HF is still rising with an estimated 64.3 million HF globally.[2] HF prevalence in China seems relatively similar compared to Western countries, ranging between 1.1% and 1.3%.[3,4] According to the data from the China Hypertension Survey ($n = 2\,2158$; 53.8% women), the estimated prevalence of HF in Chinese adults aged ≥35 years is 13.7 million (1.3%), and 1.4% had left ventricular (LV) systolic dysfunction (ejection fraction < 50%), and 2.7% had moderate or severe LV diastolic dysfunction.[3] The underlying factors include the aging of populations, the transition in low- and middle-income countries from adverse health outcomes attributable to communicable, maternal, neonatal, and nutritional causes to non-communicable diseases, and the treatment advances leading to an increased survival of patients with coronary heart disease.[1,5]

Hypertension is the predominant modifiable cardiovascular risk factor.[6,7] Proper management of hypertension is associated with a considerable decrease in the development of HF.[8–11] As evidenced by the Systolic Blood Pressure Intervention Trial (SPRINT), targeting a systolic blood pressure (SBP) of 120 mmHg compared with 140 mm Hg reduced hospitalized heart failure by 38%.[10] On the other hand, diastolic blood pressure (DBP) drives the blood flow through the epicardial arteries and the cardiac capillary network.[12,13] An excessively low diastolic blood pressure might therefore impair the myocardial perfusion and worsening of left ventricular dysfunction.[13] However, using as keywords in the title or abstract "blood pressure" AND "heart failure" AND "Chinese" combined with one of the following search terms, "mortality" OR "outcome" OR "prognosis," a literature search did not reveal any previous study examining the association of admission blood pressure with 30-day, 1-year, and long-term mortality in Chinese patients with different HF subtypes. We hypothesized that admission blood pressure might be associated with the risk of mortality in Chinese acute decompensated HF (ADHF) with different phenotypes. We investigated our hypothesis by conducting a retrospective analysis to assess whether admission blood pressure is associated with an increased risk of 30-day, 1-year, and long-term mortality in HF patients with different HF subtypes in China.

2 | METHODS

2.1 | Study participants

The present study was a single-center retrospective observational study. The cohort included 7512 HF patients hospitalized at the First Affiliated Hospital of Sun Yat-Sen University between September 16, 2013, and December 28, 2017. Long-term mortality data were obtained up to September 15, 2021. The study protocol complies with the Helsinki Declaration[14] and was approved by the Ethics Committee of the First Affiliated Hospital of Sun Yat-Sen University. The inclusion criteria: (i) patients were more than 18 years old and (ii) patients were diagnosed as ADHF. Patients were diagnosed as ADHF if they had at least one symptom (dyspnea, fatigue, or decreased exercise capacity), one sign (edema or rales), and structural and functional abnormalities on the echocardiogram or chest x-ray evidence of congestion.[15] Two independent cardiologists adjudicated the diagnosis of ADHF (J.Z., S.C.). The number of patients included in the present analysis totaled 2706 (Figure S1). Of these, 1731 had HF with preserved ejection fraction (HFpEF; EF ≥ 50%), 382 had HF with mildly reduced ejection fraction (HFmrEF; 40% < EF < 50%), and 593 had HF with reduced ejection fraction (HFrEF; EF ≤ 40%).[16–18]

2.2 | Clinical measurements

Blood pressure was measured once using the Omron HEM-7071 device on admission. Hypertension was a blood pressure of at least 140 mmHg systolic or 90 mmHg diastolic, or use of antihypertensive drugs. Body mass index was weight in kilograms divided by the height squared in meters. Diabetes mellitus was a fasting blood glucose exceeding 7.0 mmol/L (126 mg/dl) or a random plasma glucose exceeding 11.1 mmol/L (200 mg/dl) or use of antidiabetic agents.[19] Estimated glomerular filtration rate was derived from serum creatinine according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[20,21] Heart failure was diagnosed by clinicians using symptoms and signs indicative of heart failure and echocardiography.

2.3 | Echocardiography

The echocardiographic measurements were obtained within one week of the hospitalization. Echocardiography was performed using a Philips EPIQ 7C ultrasound scanner (Philips Medical Systems, Best, Netherlands) equipped with a X5-1 phased array probe (operated frequency range, 1.6–3.2 MHz) according to the recommendations of the American Society of Echocardiography.[22] The readers were blinded to clinical information. Scanning was performed in the left lateral decubitus position, with ECG simultaneously recorded. The EF was taken in the parasternal long axis view using the Teichholz method. For EF, the intra-observer correlation coefficient was .95 and the inter-observer correlation coefficient was .92.

2.4 | Clinical outcomes

Our study endpoints included all-cause mortality at 30-days, 1-year, during over 1 year of follow-up up to September 15, 2021, and overall all-cause mortality.[23] Information on vital status and all-cause mortality was obtained from the official death certificate, with further confirmation by medical records and by household contacts.

2.5 | Statistical analysis

For database management and statistical analysis, we used the R (version 4.1.2) and IBM SPSS Statistics software (SPSS 25). Baseline characteristics were summarized using frequencies and proportions for categorical variables, means with standard deviations for continuous variables, and compared by $\chi 2$ tests and analysis of variance, respectively. We normalized the distribution of the N-terminal prohormone B-type natriuretic peptide (NT-proBNP) by a logarithmic transformation.

SBP was divided into tertiles (low [< 120 mm Hg], medium [120–140 mm Hg], and high [> 140 mm Hg]). DBP was divided into tertiles (low [< 69 mm Hg], medium [69–80 mm Hg], and high [> 80 mm Hg]). The Kaplan–Meier method was used to determine cumulative probabilities of each type of mortality according to tertiles of SBP and DBP. Logistic regression and Cox regression were employed to examine the risk of 30-day, 1-year, and long-term mortality associated with 1-SD increment in SBP and DBP and with each blood pressure category. In multivariable-adjusted analyses, in line with the previous studies,[24,25] we accounted for sex, baseline characteristics age, heart rate, total serum cholesterol, blood glucose, serum creatinine, log-transformed N-terminal prohormone B-type natriuretic peptide, smoking, New York Heart Association class, diabetes mellitus, coronary heart disease, aspirin, lipid-lowering drugs, use of antihypertensive drugs by class, that is, diuretics, β-blockers, inhibitors of the renin-angiotensin, calcium-channel blockers. The fully adjusted models expressed the risk of mortality with SBP or DBP referred to the multivariable-adjusted analyses additionally accounted for DBP or SBP. We investigated the association of all-cause mortality with blood pressure in different HF subtypes. We constructed heat maps to visualize the contribution of SBP and DBP on admission in their associations with overall all-cause mortality.

3 | RESULTS

3.1 | Baseline characteristics

This analysis included 2706 patients, among whom 1057 (39.1%) patients were women, 594 (22.0%) were smokers, 1241 (45.9%) had NYHA class III or IV symptoms, 1656 (61.2%) had hypertension, 926 (34.2%) diabetes mellitus, and 1608 (59.4%) coronary heart disease. Age averaged (± SD) 68.8 ± 13.1 years, and SBP/DBP 131.2 ± 24.6 mm Hg/75.6 ± 14.4 mm Hg, respectively. Median NT-proBNP concentrations were 1365.0 (interquartile range, 648.9–3498.5) pg/ml in HFpEF, 3060.5 (interquartile range, 1368.2–7684.5) pg/ml in HFmrEF and 3645.0 (interquartile range, 1724.0–8154.0) pg/ml in HFrEF. Table 1 lists the baseline characteristics of participants by tertiles of the distributions of SBP and DBP, respectively. Compared with patients with lowest blood pressure, those with highest blood pressure had higher total and low-density lipoprotein cholesterol (Table 1). Table S1 shows the baseline characteristics of participants by HF subtypes. Compared with patients with HFrEF, those with HFpEF were more likely to be women, were older, and had a higher prevalence of hypertension (Table S1). As shown in Table S2, SBP was closely related to DBP in both HFpEF ($r = .55$; $p < .001$) and HFrEF ($r = .65$; $p < .001$).

3.2 | Association of mortality with blood pressure

During a median follow-up of 4.1 years, 1341 patients died. All-cause mortality rate was 3.5% ($n = 95$) for 30-day mortality, 16.7% ($n = 453$) for 1-year mortality, and 39.4% ($n = 888$) for long-term mortality (> 1 year).

In unadjusted models (Table 2), both SBP and DBP were significantly ($p \leq .002$) associated with 30-day mortality (odds ratio, .69; 95% confidence interval [CI], .55–.86/.64; 95% CI, .51–.80) and 1-year mortality (.84; 95% CI, .76–.94/.77; 95% CI, .70–.86). After adjusted for potential confounders, the corresponding odds ratios were .71/.65 ($p \leq .007$) for 30-day mortality and .82/.76 ($p \leq .002$) for 1-year mortality. In multivariable-adjusted analyses additionally accounted for DBP (Table 2) or SBP (Figure S2 and Table 2), a higher SBP conferred a higher risk of long-term mortality (hazard ratio [HR], 1.11; 95% CI, 1.02–1.22; $p = .017$) and DBP was associated with 30-day and 1-year mortality with odds ratio amounting to .69 (95% CI, .51–.92; $p < .001$) and .77 (95% CI, .67–.89; $p < .001$), respectively. As shown in Figure 1, compared with the top tertile of SBP and DBP, the adjusted cumulative incidence of 30-day and 1-year mortality was higher ($p \leq .021$) in the low tertile. Figure 2 visualizes the associations of SBP and DBP on admission with overall all-cause mortality. After additionally adjusted for DBP, there was no association of overall mortality with

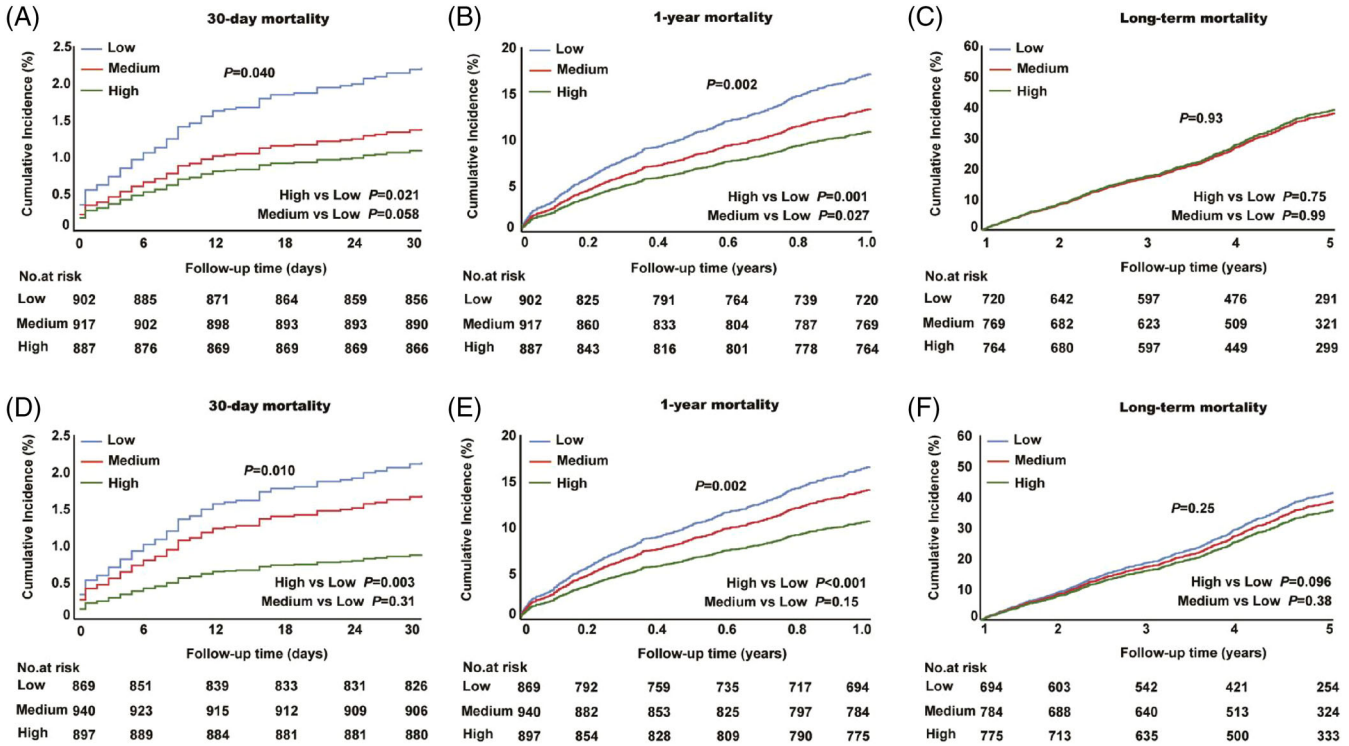

FIGURE 1 Cumulative incidence of 30 day and 1 year mortality, and long-term mortality by tertiles of systolic (A, B, and C) and diastolic blood pressure (D, E, and F). All models were adjusted for sex, the baseline characteristics age, heart rate, serum total cholesterol, blood glucose, serum creatinine, log-transformed N-terminal prohormone B-type natriuretic peptide, smoking, New York Heart Association class, diabetes mellitus, coronary heart disease, aspirin, lip-lowering drugs, use of antihypertensive drugs by class, that is, diuretics, β-blockers, inhibitors of the renin-angiotensin, and calcium-channel blocker. The 30 day and 1 year mortality, and long-term mortality rate were 3.5%, 16.7%, and 39.4%

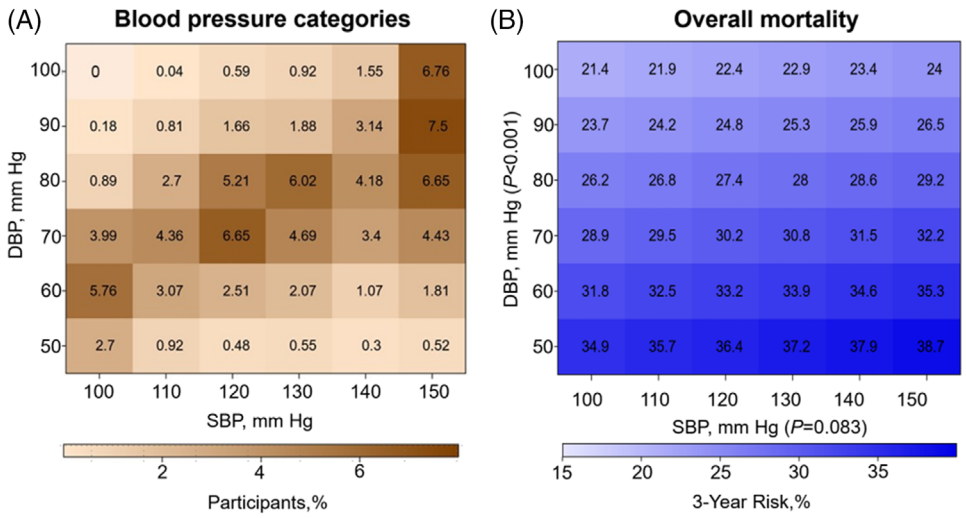

FIGURE 2 Heat maps depicting 3-year risk of mortality in relation to systolic and diastolic blood pressure. Estimates of 3-year risk were standardized to the average of the distributions in the whole study population (mean or ratio) of all covariables. Numbers in the panel A grid represent the percentage of participants within each BP cross-classification category; numbers in the B grid represent the 3-year risk of mortality. SBP indicates systolic blood pressure; DBP, diastolic blood pressure

TABLE 1 Baseline characteristics of participants by tertiles of systolic and diastolic blood pressure

	SBP (mmHg)				DBP (mmHg)			
Characteristic	**<120**	**120–140**	**>140**	***p*-value**	**<69**	**69–80**	**>80**	***p*-value**
Number (%) with characteristic	902	917	887		869	940	897	
Women	323 (35.8)	346 (37.7)	388 (43.7)	.002	343 (39.5)	370 (39.4)	344 (38.4)	.87
Current smoker	225 (24.9)	202 (22.0)	167 (18.8)	.008	181 (20.8)	202 (21.5)	211 (23.5)	.36
Coronary heart disease	478 (53.0)	567 (61.8)	563 (63.5)	<.001	537 (61.8)	572 (60.9)	499 (55.6)	.017
Hypertension	336 (37.3)	555 (60.5)	765 (86.2)	<.001	442 (50.9)	565 (60.1)	649 (72.4)	<.001
Diabetes	257 (28.5)	306 (33.4)	363 (40.9)	<.001	292 (33.6)	333 (35.4)	301 (33.6)	.63
Atrial fibrillation	262 (29.0)	266 (29.0)	160 (18.0)	<.001	208 (23.9)	234 (24.9)	246 (27.4)	.22
NYHA class III or IV	434 (48.1)	403 (43.9)	404 (45.5)	.20	412 (47.4)	417 (44.4)	412 (45.9)	.43
ACEI/ARB	682 (75.6)	735 (80.2)	776 (87.5)	<.001	655 (75.4)	757 (80.5)	781 (87.1)	<.001
β-Blocker	783 (86.8)	782 (85.3)	736 (83.0)	.073	723 (83.2)	802 (85.3)	776 (86.5)	.14
CCB	61 (6.8)	140 (15.3)	339 (38.2)	<.001	122 (14.0)	180 (19.1)	238 (26.5)	<.001
Diuretics	672 (74.5)	638 (69.6)	646 (72.8)	.058	641 (73.8)	646 (68.7)	669 (74.6)	.01
Spironolactone	638 (70.7)	582 (63.5)	508 (57.3)	<.001	566 (65.1)	580 (61.7)	582 (64.9)	.23
Lipid-lowering drugs	650 (72.1)	760 (82.9)	767 (86.5)	<.001	689 (79.3)	768 (81.7)	720 (80.3)	.43
Aspirin	492 (54.5)	538 (58.7)	530 (59.8)	.062	492 (56.6)	555 (59.0)	513 (57.2)	.55
Mean (± SD) of characteristic								
Age (years)	64.4 ± 14.1	69.9 ± 12.2	72.1 ± 11.8	<.001	69.7 ± 13.5	69.0 ± 12.6	67.8 ± 13.3	.008
SBP (mm Hg)	105.7 ± 10.1	129.5 ± 6.2	158.9 ± 16.4	<.001	116.9 ± 22.2	129.5 ± 19.5	146.8 ± 22.5	<.001
DBP (mm Hg)	66.8 ± 11.0	75.8 ± 11.5	84.2 ± 14.7	<.001	60.4 ± 6.5	74.4 ± 3.5	91.5 ± 9.5	<.001
Heart rate (beats per min)	84.0 ± 20.5	83.9 ± 20.6	80.3 ± 18.4	<.001	77.8 ± 18.0	82.6 ± 19.3	87.7 ± 21.2	<.001
Total cholesterol (mmol/L)	4.1 ± 1.2	4.2 ± 1.2	4.5 ± 1.3	<.001	4.1 ± 1.2	4.3 ± 1.2	4.5 ± 1.3	<.001
LDL cholesterol (mmol/L)	2.6 ± .8	2.7 ± .9	2.9 ± 1.0	<.001	2.5 ± .9	2.7 ± .9	2.9 ± .9	<.001
Glucose (mmol/L)	7.0 ± 3.5	7.2 ± 3.5	7.7 ± 4.0	.001	7.2 ± 3.8	7.3 ± 3.6	7.3 ± 3.6	.90
eGFR (ml/min/1.73 m2)	68.3 ± 26.3	62.3 ± 26.3	53.6 ± 27.3	<.001	60.0 ± 27.4	61.6 ± 27.9	62.7 ± 26.5	.11

eGFR was derived from serum creatinine according to the Chronic Kidney Disease Epidemiology Collaboration.

p values denote the significance of the between-group differences.

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CCBs, calcium-channel blockers; DBP, diastolic blood pressure; LDL, low-density lipoprotein; NYHA, New York Heart Association. SBP, systolic blood pressure.

SBP ($p = .083$; Figure 2B). Compared with HF patients with top tertile of DBP, those with low tertile of DBP had ahigher risk of overall all-cause mortality ($p \leq .001$; Table 2 and Figure S3). In patients with DBP > 80 mm Hg, a higher SBP predicted a higher risk of long-term mortality (HR, 1.19; 95% CI, 1.00–1.41; $p = .049$; Table S3). Sensitivity analyses stratified by sex (Table S4), median of age (Table S5), status of hypertension (Table S6), and status of atrial fibrillation (Table S7) confirmed the association of mortality with blood pressure.

3.3 | Association of mortality with blood pressure by HF subtypes

In patients with HFpEF (Table 3), a higher SBP was associated with a higher risk of long-term mortality (HR, 1.22; 95% CI, 1.12–1.32; $p < .001$). After adjustments applied for potential confounders including DBP (Table 3), the associations of long-term mortality with SBP remained significant (HR 1.16; 95% CI, 1.04–1.29; $p = .007$). In patients with HFmrEF and HFrEF (Table 3), SBP was significantly ($p \leq .012$) associated with 1-year mortality in both unadjusted models (odds ratio, .72; 95% CI, .55–.93/.69; 95% CI, .54–.88) and multivariable-adjusted models (odds ratio, .54; 95% CI, .38–.75/.63; 95% CI, .46–.86), while lost significance in adjusted models additionally accounted for DBP (Table 3).

In patients with HFpEF (Table 4), independent of potential confounders including SBP, DBP was significantly associated with long-term mortality (HR, .89; 95% CI, .80–.99; $p = .028$). In patients with HFmrEF and HFrEF (Table 4), irrespective of adjustments of potential confounders, DBP was associated with risk of 1-year mortality with odds ratios ranging from .49 to .62 ($p \leq .006$).

TABLE 2 Risk of mortality associated with blood pressure components

		Unadjusted models		Adjusted models		Fully adjusted models	
Model	*n* (death)	Estimate (95% CI)	*p*-value	Estimate (95%CI)	*p*-value	Estimate (95%CI)	*p*-value
Systolic pressure categories							
Overall mortality							
<120 mm Hg	902 (429)	ref		ref			
120–140 mm Hg	917 (446)	.98 (.86–1.12)	.79	.91 (.80–1.04)	.18	1.00 (.87–1.16)	.95
>140 mm Hg	887 (466)	1.06 (.93–1.21)	.37	.88 (.76–1.01)	.077	1.05 (.89–1.24)	.57
Systolic pressure (+1-SD)							
Overall mortality	2706 (1341)	1.04 (.98–1.09)	.19	.96 (.91–1.02)	.22	1.07 (.99–1.15)	.083
30-day mortality	2706 (95)	.69 (.55–.86)	<.001	.71 (.55–.91)	.007	.89 (.66–1.21)	.47
1-year mortality	2706 (453)	.84 (.76–.94)	.002	.82 (.72–.93)	.002	.96 (.83–1.12)	.64
Long-term mortality	2253 (888)	1.14 (1.07–1.22)	<.001	1.03 (.96–1.11)	.38	1.11 (1.02–1.22)	.017
Diastolic pressure categories							
Overall mortality							
<69 mm Hg (ref)	869 (471)	ref		ref			
69–80 mm Hg	940 (465)	.85 (.74–.96)	.010	.90 (.79–1.03)	.13	.90 (.78–1.02)	.11
>80 mm Hg	897 (405)	.74 (.64–.84)	<.001	.78 (.68–.90)	.001	.76 (.65–.90)	.001
Diastolic pressure (+1-SD)							
Overall mortality	2706 (1341)	.86 (.81–.91)	<.001	.88 (.83–.93)	<.001	.85 (.79–.91)	<.001
30-day mortality	2706 (95)	.64 (.51–.80)	<.001	.65 (.51–.82)	<.001	.69 (.51–.92)	.011
1-year mortality	2706 (453)	.77 (.70–.86)	<.001	.76 (.67–.85)	<.001	.77 (.67–.89)	<.001
Long-term mortality	2253 (888)	.90 (.84–.96)	.002	.94 (.87–1.01)	.070	.88 (.81–.96)	.004

Estimates (95% confidence interval) express the odds ratio of 30-day and 1-year mortality and hazards ratio of long-term and total mortality associated with systolic and diastolic blood pressure, respectively. Adjusted models were adjusted for sex, the baseline characteristics age, heart rate, serum total cholesterol, blood glucose, serum creatinine, log-transformed N-terminal prohormone B-type natriuretic peptide, smoking, New York Heart Association class, diabetes mellitus, coronary heart disease, aspirin, lip-lowering drugs, use of antihypertensive drugs by class, that is, diuretics, β-blockers, inhibitors of the renin-angiotensin, and calcium-channel blocker. The fully adjusted models additionally accounted for diastolic or systolic blood pressure.

4 | DISCUSSION

In the current study, we systematically investigated the associations of 30-day, 1-year, and long-term mortality with SBP and DBP on admission in a large-scale population of HF patients with different HF subtypes. The key findings of our study can be summarized as follows: (i) in HF patients, a higher SBP was associated with a higher risk of long-term mortality and a lower DBP was associated with the increased risk of all types of mortality, irrespective of adjustments of potential confounders including DBP or SBP on admission; (ii) in HFpEF, higher SBP and lower DBP levels were significantly associated with a higher risk of long-term mortality; and (iii) in HFmrEF and HFrEF, a lower DBP was significantly associated with a higher risk of 1-year mortality, independent of potential confounders including admission SBP.

Several previous studies investigated the associations of mortality with SBP or DBP.[26–30] Among 7599 patients (Women, 31.6%; mean age, 65.5 years) with chronic HF in the CHARM programme, during a median follow-up of 38 months, 1831 died.[26] 1-SD decrease in DBP was associated with high risk of all-cause mortality (adjusted HR, 1.10; 95% CI, 1.05–1.15).[26] In 5747 HF patients (Women, 23%; mean age, 63.0 years) from the Digitalis Investigation Group trial, during a median follow-up of 38 months, 2066 patients died.[27] Compared with patients with blood pressure of 130–139 mm Hg, those with lower SBP (< 100 mm Hg) had a higher risk of all-cause mortality (adjusted HR, 1.80; 95% CI, 1.36–2.38).[27] Compared with a SBP level of 80–89 mm Hg, DBP < 60 mm Hg was associated with a higher risk of all-cause mortality (adjusted HR, 1.64; 95% CI, 1.23–2.18).[27] Among 10 979 acute HF patients (Women, 55.6%; mean age, 80.4 years) from 41 Spanish emergency departments, 1143 patients died within the first 30 days.[28] The 30-day mortality rates were 35.4%, 18.9%, 12.4%, and 7.5% for SBP < 90 mm Hg, 90–109 mm Hg, 110–129 mm Hg, and ≥130 mm Hg.[28] Compared with SBP > 130 mm Hg, SBP < 90 mm Hg was associated with a higher risk of 30-day mortality (OR, 6.71; 4.82–9.35).[28] Zhang and colleagues conducted a meta-analysis to investigate quantitatively the association between SBP on admission and all-cause mortality in 133 549 HF patients from 15 studies.[29] Meta analysis from 6 studies demonstrated that compared with higher SBP groups, the lowest SBP was associated with higher risk (HR, 2.22; 95% CI, 1.72–2.86) of all-cause mortality.[29] However, those studies did not compare associations of mortality with SBP versus DBP. In our study, independent of admission DBP, a higher SBP on admission was associated with a higher risk of long-term mortality, while in adjusted analyses

TABLE 3 Risk of 30-day, 1-year, and long-term mortality associated with systolic blood pressure by heart failure subtypes

		Unadjusted models		Adjusted models		Fully adjusted models	
Model	***n* (death)**	**Estimate (95%CI)**	***p*-value**	**Estimate (95%CI)**	***p*-value**	**Estimate (95%CI)**	***p*-value**
HFpEF ($n = 1731$)							
Overall mortality	1731 (819)	1.15 (1.08–1.24)	<.001	1.05 (.98–1.14)	.17	1.13 (1.03–1.24)	.008
30-day mortality	1731 (46)	.70 (.51–.97)	.030	.68 (.48–.96)	.030	.78 (.51–1.19)	.25
1-year mortality	1731 (240)	1.03 (.90–1.18)	.69	1.00 (.85–1.17)	.98	1.07 (.88–1.29)	.52
Long-term mortality	1491 (579)	1.22 (1.12–1.32)	<.001	1.09 (.99–1.19)	.077	1.16 (1.04–1.29)	.007
HFmrEF ($n = 382$)							
Overall mortality	382 (204)	.96 (.84–1.10)	.54	.82 (.70–.96)	.014	.97 (.80–1.17)	.72
30-day mortality	382 (20)	.76 (.46–1.23)	.26	.54 (.26–1.13)	.10	.78 (.34–1.80)	.56
1-year mortality	382 (87)	.72 (.55–.93)	.012	.54 (.38–.75)	<.001	.75 (.50–1.13)	.16
Long-term mortality	295 (117)	1.12 (.95–1.32)	.19	1.02 (.83–1.24)	.87	1.07 (.83–1.38)	.61
HFrEF ($n = 593$)							
Overall mortality	593 (318)	.87 (.77–.99)	.040	.83 (.72–.95)	.009	1.03 (.85–1.24)	.79
30-day mortality	593 (29)	.74 (.47–1.16)	.18	.70 (.42–1.17)	.17	1.08 (.53–2.17)	.83
1-year mortality	593 (126)	.69 (.54–.88)	.003	.63 (.46–.86)	.004	.99 (.66–1.50)	.97
Long-term mortality	467 (192)	.98 (.84–1.15)	.84	.91 (.75–1.10)	.31	1.03 (.80–1.32)	.84

Estimates (95% confidence interval) express the odds ratio of 30-day and 1-year mortality and hazards ratio of long-term mortality and total mortality associated with 1-SD increment in systolic blood pressure, respectively. Adjusted models were adjusted for sex, the baseline characteristics age, heart rate, serum total cholesterol, blood glucose, serum creatinine, log-transformed N-terminal prohormone B-type natriuretic peptide, smoking, New York Heart Association class, diabetes mellitus, coronary heart disease, aspirin, lip-lowering drugs, use of antihypertensive drugs by class, that is, diuretics, β-blockers, inhibitors of the renin-angiotensin, and calcium-channel blocker. The fully adjusted models additionally accounted for diastolic blood pressure.

TABLE 4 Risk of 30-day, 1-year, and long-term mortality associated with diastolic blood pressure by heart failure subtypes

		Unadjusted models		Adjusted models		Fully adjusted models	
Model	***n* (death)**	**Estimate (95%CI)**	***p*-value**	**Estimate (95%CI)**	***p*-value**	**Estimate (95%CI)**	***p*-value**
HFpEF ($n = 1731$)							
Overall mortality	1731 (819)	.91 (.85–.98)	.011	.95 (.88–1.02)	.15	.88 (.81–.97)	.007
30–day mortality	1731 (46)	.66 (.48–.91)	.012	.69 (.49–.97)	.032	.79 (.52–1.2)	.26
1-year mortality	1731 (240)	.92 (.80–1.06)	.23	.92 (.79–1.08)	.32	.89 (.74–1.08)	.24
Long-term mortality	1491 (579)	.91 (.83–.99)	.027	.96 (.88–1.05)	.38	.89 (.80–.99)	.028
HFmrEF ($n = 382$)							
Overall mortality	382 (204)	.79 (.69–.91)	.001	.76 (.65–.88)	<.001	.77 (.64–.94)	.009
30-day mortality	382 (20)	.56 (.34–.91)	.019	.46 (.23–.92)	.028	.51 (.23–1.12)	.093
1-year mortality	382 (87)	.60 (.46–.78)	<.001	.49 (.35–.69)	<.001	.58 (.39–.85)	.006
Long-term mortality	295 (117)	.91 (.76–1.08)	.29	.96 (.79–1.17)	.72	.93 (.72–1.19)	.55
HFrEF ($n = 593$)							
Overall mortality	593 (318)	.78 (.70–.87)	<.001	.78 (.69–.88)	<.001	.77 (.66–.90)	.001
30-day mortality	593 (29)	.65 (.43–.98)	.040	.60 (.38–.96)	.035	.58 (.31–1.09)	.088
1-year mortality	593 (126)	.62 (.50–.77)	<.001	.57 (.43–.74)	<.001	.57 (.40–.80)	.001
Long-term mortality	467 (192)	.86 (.75–.98)	.027	.88 (.75–1.02)	.086	.86 (.71–1.06)	.16

Estimates (95% confidence interval) express the odds ratio of 30-day and 1-year mortality and hazards ratio of long-term mortality and total mortality associated with 1-SD increment in diastolic blood pressure, respectively. Adjusted models were adjusted for sex, the baseline characteristics age, heart rate, serum total cholesterol, blood glucose, serum creatinine, log-transformed N-terminal prohormone B-type natriuretic peptide, smoking, New York Heart Association class, diabetes mellitus, coronary heart disease, aspirin, lip-lowering drugs, use of antihypertensive drugs by class, that is, diuretics, β-blockers, inhibitors of the renin-angiotensin, and calcium-channel blocker. The fully adjusted models additionally accounted for systolic blood pressure.

additionally accounted for admission SBP, a lower DBP on admission was associated with all types of mortality.

Furthermore, we investigated the association of 30-day, 1-year, and long-term mortality with admission SBP and DBP in Chinese HF patients with different HF subtypes. Several previous studies investigated the association of short-term or long-term mortality with SBP or DBP in patients with HFpEF[23,31,32] or HFrEF.[33–35] Among 1802 propensity score-matched HFpEF patients (Women, 63.7%; mean age, 79.0 years; EF ≥50%) from the Medicare-linked Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) registry,[23] the 30-day and 1-year mortality rate were 10% and 39% for discharge SBP < 120 mm Hg and 5% and 31% for SBP ≥120 mm Hg, respectively. SBP < 120 mm Hg was associated with higher risk of 30-day mortality (HR, 2.07; 95% CI, 1.45–2.95), 1-year mortality (HR, 1.36; 95% CI, 1.16–1.59), and mortality during a median follow-up of 2.1 years (HR, 1.17; 95% CI, 1.05–1.30) with reference of SBP ≥120 mm Hg.[23] In 1703 HFpEF patients (Women, 50%; mean age, 72.0 years; EF ≥45%) enrolled in the Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist (TOPCAT) trial,[31] during a median follow-up of 2.9 years, 372 deaths occurred. Compared with DBP of 60–69 mm Hg, DBP of < 60 mm Hg was associated with higher risk of total death (HR, 1.68; 95% CI, 1.21–2.33).[31] However, there was no significant association between SBP and all-cause mortality in the TOPCAT trial. In 3538 HFrEF patients (Women, 44.1%; mean age, 67.4 years; EF ≥45%) of three Korean observational studies, per 10 mm Hg increase in SBP was associated with reduced risk of 1-year mortality (HR, .915; 95% CI, .853–.981).[33] In our Chinese ADHF patients, we demonstrated that in HFpEF patients, both SBP and DBP on admission were associated with long-term mortality and in HFmrEF and HFrEF patients, a lower DBP was significantly associated with a higher risk of 1-year mortality, highlighting the importance of admission blood pressure in risk stratification.

To the best of our knowledge, our current study is the first to systematically assess the associations of the risk of 30-day, 1-year, and long-term mortality with SBP and DBP among patients with HFpEF, HFmrEF, or HFrEF from the same population in China. These findings highlight the importance of admission blood pressure in risk stratification, particularly for all-cause mortality in ADHF patients. Our previous study found that the long-term exposure of blood pressure as exemplified by blood pressure variability was associated with adverse health outcomes over and beyond blood pressure levels in patients with HFpEF. The clinical significance of admission blood pressure might be different from blood pressure in chronic phase.[36] Furthermore, our study is distinguished by a relatively large sample size, the use of an EF ≥50% to define HFpEF, and consistent observations irrespective of adjustment for potential confounders, subgroup analyses, and sensitivity analyses. We also demonstrated that more drugs were used in the higher blood pressure group (Table 1), indicating lower blood pressure in this study might be the natural disease course or the consequence of the comorbidity rather than driven by more drug administration. Our current study should be interpreted within the context of its possible limitations. First, regarding the observational nature of our study, missing variables and residual confounding factors may influence the results. For instance, we fail to precisely calculate the Charlson Comorbidity Index, indicating comorbidity conditions.[37] Second, the number of patients with HFrEF was relatively small, which might weaken the associations between the risk of mortality and blood pressure. In our study, the EF measured by the Teichholz method may be not accurate for the patients with regional wall motion abnormality due to prior myocardial infarction or other diseases, in whom the EF may be overestimated. Therefore, patients with HFmrEF or HFrEF could be mis-classified as HFpEF. That's why HFpEF outnumbered the other 2 HF subtypes. Third, our current findings in Chinese patients cannot be extrapolated to other ethnicities. Finally, some patients with NT-proBNP < 300 pg/ml were excluded from the current analysis (Figure S1). However, compared with patients with NT-proBNP ≥300 pg/ml, those with NT-proBNP < 300 pg/ml had similar proportion of women ($p = .24$), but were on average 3.7 years younger ($p < .001$), and had a slightly higher SBP (133.2 mm Hg vs. 131.2 mm Hg; $p = .001$) and DBP (76.9 mm Hg vs. 75.6 mm Hg; $p < .001$).

5 | CONCLUSIONS

In Chinese patients with different HF subtypes, higher SBP, and lower DBP levels were associated with higher risk of different types of mortality. From a clinical point of view, our current study underlines that admission blood pressure may have crucial implications for risk assessment in Chinese patients with different HF subtypes, particularly for all-cause mortality.

AUTHOR CONTRIBUTIONS

Yugang Dong, Chen Liu, and Fang-Fei Wei contributed to conception and design, interpretation of data, and drafted the manuscript. Jan A. Staessen and Jiangui He contributed to conception, interpretation of data, and critically revised the manuscript. Shilan Chen, Weihao Liang, Yuzhong Wu, Xuwei Chen, Xin He and Jingjing Zhao contributed to data acquisition, analysis and draft the manuscript. All authors gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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