ORIGINAL RESEARCH ARTICLE

Systolic blood pressure at admission and long-term clinical outcomes in patients hospitalized for heart failure

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Abstract

Aims   The study sought to investigate the association between admission systolic blood pressure (SBP) and 1-year clinical outcomes in patients hospitalized for heart failure (HF) and in subgroups.

Methods   This study was based on the China Patient-centred Evaluative Assessment of Cardiac Events Prospective Heart Failure Study, which prospectively enrolled patients hospitalized for HF in 52 hospitals from 20 provinces in China between August 2016 and May 2018. Patients were divided into four groups according to the quartiles of SBP at admission. The multivariable Cox proportional hazards regression models were fitted to examine the association between admission SBP and all-cause death and HF readmission within 1 year after the index hospitalization. Restricted cubic splines were used to explore the non-linear association between SBP and the clinical outcomes.

Results   Among 4896 patients, those with lower admission SBP were younger, more likely to be male, have left ventricular ejection fraction <40%, and receive β-blockers, aldosterone antagonists, and diuretics. After adjustment for potential confounders, lower admission SBP was significantly associated with higher all-cause death and there is no threshold, while we only observed such an association with HF readmission when admission SBP was lower than 120 mmHg. Compared with the 4th SBP quartile, patients in the 1st SBP quartile had higher risk of all-cause death (hazard ratio, 1.85; 95% confidence interval 1.48–2.33; *P* < 0.001) and HF readmission (hazard ratio, 1.40; 95% confidence interval 1.19–1.65, *P* < 0.001). These associations were consistent in most subgroups, such as age, sex, and left ventricular ejection fraction.

Conclusions   In patients hospitalized for HF, lower admission SBP portends an increased risk of 1 year all-cause death and HF readmission, and these associations were consistent among subgroups.

Introduction

Heart failure (HF) is a global major public health problem due to its high prevalence and poor prognosis.[1] Approximately 64.3 million people suffer from HF globally, and the prevalence is increasing with extended longevity, high prevalence of risk factors, and improved survival in those with cardiovascular disease.[1–3] High blood pressure is associated with an increased risk of the development of HF,[4–6] and about 50% of

patients admitted to hospital for HF have elevated systolic blood pressure (SBP).[7,8] Patients hospitalized for HF are at high risk for all-cause death and HF readmission.[9,10] It is important to understand the association between SBP at admission and long-term outcomes of HF patients.

Previous studies demonstrated that acute HF patients with lower admission SBP had higher risk of short-term death[8,11–13]; however, inconsistent results have been found in the association between admission SBP and long-term

death, particularly whether the continuous relationship between lower admission SBP and higher mortality exists without upper threshold.[8,13–16] Despite the high frequency of HF readmission, little is known about the association between admission SBP and HF readmission during the first year after the index hospitalization.[14,17] Besides, patients with HF is a heterogeneous population and some studies indicated discrepancy in the association between admission SBP and prognosis among important subgroups [e.g. left ventricular ejection fraction (LVEF), diabetes, and age], which requires further investigation.[8,14–17]

To address this issue, we examined the association between admission SBP and 1 year clinical outcomes in a large prospective multicentre cohort of patients hospitalized for HF, and the associations in important subgroups as well.

Methods

Study design and population

We established a nationwide prospective cohort of acute HF, the China Patient-centered Evaluative Assessment of Cardiac Events Prospective Heart Failure Study (China PEACE 5p-HF Study), from 52 hospitals located in 20 provinces, covering all economic-geographic regions in China; the study design has been published before.[18] Patients were eligible if they were aged 18 years or older, local residents, and hospitalized primarily for new-onset HF or decompensation of chronic HF. Between August 2016 and May 2018, we consecutively screened eligible patients and enrolled them if they signed informed consent to participate the study within 48 h of admission. We interviewed enrolled patients to collect data during the index hospitalization and at 1 month, 6 months, and 1 year after discharge.

The China PEACE 5p-HF study was approved by the ethics committees of Fuwai Hospital and all collaborating hospitals. The study protocol was registered on ClinicalTrials.gov (number: NCT02878811).

Data collection

We collected information on demographic characteristics, socio-economic characteristics, smoking status, and self-reported health status using a standardized questionnaire through face-to-face interview by trained local clinicians during index hospitalization. Data were directly entered into laptop computers equipped with a customized electronic data collection system to allow real-time off-line logic checks to verify the accuracy and completeness of entered data. We obtained clinical status, comorbidities, and medications through central medical record abstraction. LVEF was measured during hospitalization by trained clinicians according

to the standard echocardiogram protocol. Laboratory test of serum creatinine, HbA_{1c}, low-density lipoprotein cholesterol, and N-terminal pro-brain natriuretic peptide (NT-proBNP) were based on central laboratory tests (i.e. tests of blood and urine samples taken within 48 h of admission) or local laboratory tests at admission if central laboratory tests were unavailable (missing rate <7%); haemoglobin was based on local admission laboratory test results.

If patients had HF for some time and chronic stable HF deterioration led to the admission, they were considered as decompensation of chronic HF; others were considered as new-onset HF. Coronary heart disease, hypertension, diabetes, chronic obstructive pulmonary disease, valvular heart disease, stroke, atrial fibrillation, reduced renal function, and anaemia were defined according to medical history, discharge diagnosis, or positive laboratory test results. The diagnosis criteria of laboratory tests of anaemia (haemoglobin <120 g/L in men or <110 g/L in women), reduced renal function (estimated glomerular filtration rate <60 mL/min/ 1.73 m²), and diabetes ($HbA_{1c} \geq 6.5\%$) were defined. Self-reported health status was evaluated during index hospitalization by the summary score of the short version of the Kansas City Cardiomyopathy Questionnaire, with scores ranging from 0 to 100 (lower score indicating poorer health status).

Outcomes

Two clinical outcomes were evaluated: all-cause death and HF readmission within 1 year after the index hospitalization. We collected information on clinical outcomes through follow-up interviews and searching the national death cause database in China. Potential outcome events were centrally adjudicated based on medical records by trained clinicians at the national coordinating centre.

Statistical analysis

Patient characteristics were described using mean ± standard deviation, median (interquartile range), or frequency (percentage) as appropriate. Patients were categorized into quartiles by admission SBP (<117, 117–130, 131–148, and >148 mmHg). We evaluated the differences in baseline characteristics of patients among the SBP groups using the one-way analysis of variance for normal distributed continuous variables, the Kruskal–Wallis test for skewed distributed continuous variables, and the chi-square test for categorical variables.

Kaplan–Meier survival analysis was used to compare cumulative risk of outcomes. Differences in outcomes across SBP groups were evaluated using the log-rank test. The associations between SBP and outcomes were estimated with Cox

proportional hazards regression models, adjusting demographic characteristics (age and sex), socio-economic status (marital status and education level), clinical characteristics at admission (body mass index, heart rate, New York Heart Association functional class, LVEF, and HF type), current smoking, comorbidities (coronary heart disease, hypertension, diabetes, chronic obstructive pulmonary disease, valvular heart disease, stroke, atrial fibrillation, reduced renal function, and anaemia), laboratory test results at admission (low-density lipoprotein cholesterol, NT-proBNP), medications before admission [angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), β-blockers, aldosterone antagonists, and diuretics], medications during hospitalization (ACEIs, ARBs, β-blockers, aldosterone antagonists, diuretics, digoxin, and nitrates), and Kansas City Cardiomyopathy Questionnaire sum score. Restricted cubic splines were used to explore the non-linear association between SBP and the clinical outcomes. Four knots were placed at the 5th, 35th, 65th, and 95th percentiles (at 97, 121, 140, and 180 mmHg, respectively).

We conducted subgroup analyses to assess the homogeneity of the association between SBP and outcomes in clinical important subgroups, including sex (male or female), age (<65 or ≥65 years), LVEF (<40%, 40–49%, or ≥50%), HF type (new-onset HF or decompensation of chronic HF), NT-proBNP (<median or ≥median), diabetes (yes or no), atrial fibrillation (yes or no), coronary heart disease (yes or no), valvular heart disease (yes or no), prescriptions of ACEIs/ARBs (yes or no), β-blockers (yes or no), and aldosterone antagonists (yes or no).

Variables with missing values (e.g. NT-proBNP and Kansas City Cardiomyopathy Questionnaire score) were imputed using the multiple imputation method with 20 imputations, and the final imputed value was the average of the 20 imputations. NT-proBNP had the highest missing rates (112, 2.3%).

All analyses were performed with SAS (9.4, SAS institute, Cary, North Carolina, USA). All the tests of significance were two sided, and an alpha level of less than 0.05 indicated statistical significance for all analysis.

Results

Baseline characteristics

In this study, we excluded patients without admission SBP (n = 2) or patients discharged alive but not attending follow up interview (n = 9), and a total of 4896 patients were included in the current study (*Figure 1*). The mean age of patients was 65.2 ± 13.5 years, 37.6% were female, and 70.7% were decompensated chronic HF. Compared with patients with higher admission SBP, those with lower admission SBP were younger, more likely to be male, LVEF <40%, and have lower creatinine; while they were less likely to be new-onset HF, and have history of coronary heart disease, hypertension, diabetes, reduced renal function, and stroke. Prescriptions of β-blockers, aldosterone antagonists, diuretics, and digoxin during hospitalization were more often observed in the lower SBP quartiles, whereas ACEIs/ARBs and nitrates were less prescribed (*Table 1*).

Admission systolic blood pressure and clinical outcomes

Within 1 year after the index hospitalization, 856 (17.5%) patients died and 1560 (31.9%) had HF readmission. Cumulative risks for 1 year all-cause death and HF readmission by SBP groups were shown in *Figure 2*. Of patients with SBP in the

Figure 1 Flowchart of patient selection. HF, heart failure; SBP, systolic blood pressure.
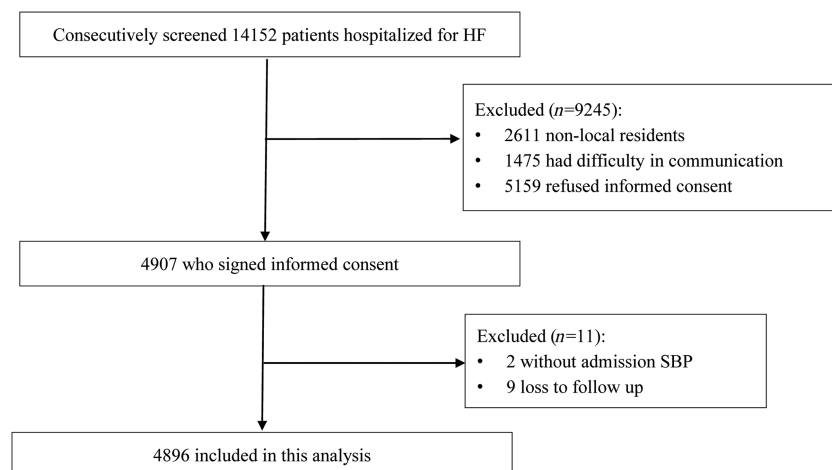
Table 1 Baseline characteristics of patients by systolic blood pressure quartiles

	Total	Q1 (SBP <117 mmHg)	Q2 (SBP 117–130 mmHg)	Q3 (SBP 131–148 mmHg)	Q4 (SBP >148 mmHg)	P value
	N = 4896	n = 1232	n = 1015	n = 1397	n = 1252	
Demographics						
Age (years)	65.2 ± 13.5	61.3 ± 13.8	65.3 ± 12.7	66.6 ± 12.9	67.5 ± 13.5	<0.001
Female	1843 (37.6)	416 (33.7)	358 (35.3)	560 (40.1)	509 (40.7)	<0.001
Socio-economic status						
Education level						0.043
Illiterate/primary school	519 (10.6)	161 (13.1)	98 (9.7)	143 (10.2)	117 (9.4)	
Junior/senior high school	2185 (44.6)	554 (44.9)	476 (46.9)	599 (42.9)	556 (44.4)	
College/postgraduate	2041 (41.7)	481 (39.0)	408 (40.2)	614 (44.0)	538 (43.0)	
Unknown	151 (3.1)	36 (2.9)	33 (3.3)	41 (2.9)	41 (3.3)	
Marital status						<0.001
Married	3830 (78.2)	1007 (81.7)	809 (79.7)	1079 (77.2)	935 (74.7)	
Divorced/separated/widowed	838 (17.1)	161 (13.1)	158 (15.6)	261 (18.7)	258 (20.6)	
Single	228 (4.7)	64 (5.2)	48 (4.7)	57 (4.1)	59 (4.7)	
Clinical status						
Medical history						
Hypertension	2857 (58.4)	382 (31.0)	491 (48.4)	898 (64.3)	1086 (86.7)	<0.001
Coronary heart disease	2840 (58.0)	571 (46.3)	582 (57.3)	875 (62.6)	812 (64.9)	<0.001
Diabetes	1539 (31.4)	305 (24.7)	296 (29.2)	473 (33.9)	465 (37.2)	<0.001
Chronic obstructive pulmonary disease	953 (19.5)	207 (16.8)	202 (19.9)	305 (21.8)	239 (19.1)	0.013
Valvular heart disease	800 (16.3)	252 (20.4)	201 (19.8)	215 (15.4)	132 (10.6)	<0.001
Stroke	1002 (20.4)	196 (15.9)	172 (17.0)	297 (21.3)	337 (26.9)	<0.001
Atrial fibrillation	1783 (36.4)	484 (39.3)	416 (41.0)	521 (37.3)	362 (28.9)	<0.001
Anaemia	1150 (23.5)	276 (22.4)	219 (21.6)	323 (23.1)	332 (26.5)	0.025
Reduced renal function	1419 (29.0)	311 (25.2)	262 (25.8)	387 (27.7)	459 (36.7)	<0.001
SBP at admission (mmHg)	133.2 ± 24.7	104.5 ± 8.7	122.3 ± 3.3	137.1 ± 5.3	165.9 ± 16.6	<0.001
DBP at admission (mmHg)	81.0 ± 16.0	69.5 ± 10.0	76.5 ± 11.0	83.0 ± 12.7	93.8 ± 17.5	<0.001
HR at admission (beats/min)	89.3 ± 22.4	89.8 ± 23.2	88.2 ± 21.7	89.7 ± 22.2	89.5 ± 22.4	0.285
NYHA class at admission						<0.001
II	705 (14.4)	152 (12.3)	172 (16.9)	203 (14.5)	178 (14.2)	
III	2163 (44.2)	519 (42.1)	498 (49.1)	640 (45.8)	506 (40.4)	
IV	2028 (41.4)	561 (45.5)	345 (34.0)	554 (39.7)	568 (45.4)	
LVEF type						<0.001
LVEF<40%	1850 (37.8)	641 (52.0)	390 (38.4)	494 (35.4)	325 (26.0)	
LVEF 40–49%	1041 (21.3)	229 (18.6)	226 (22.3)	296 (21.2)	290 (23.2)	
LVEF ≥50%	1706 (34.8)	297 (24.1)	341 (33.6)	518 (37.1)	550 (43.9)	
Unmeasured	299 (6.1)	65 (5.3)	58 (5.7)	89 (6.4)	87 (6.9)	
HF type						<0.001
New-onset HF	1440 (29.4)	277 (22.5)	250 (24.6)	428 (30.6)	485 (38.7)	
Decompensated chronic HF						
Hospitalized in prior half year	458 (9.4)	143 (11.6)	106 (10.4)	115 (8.2)	94 (7.5)	
Without hospitalization in prior half year	2998 (61.3)	812 (65.9)	659 (64.9)	854 (61.1)	673 (53.8)	
Body mass index (kg/m^2)						<0.001
<18.5	343 (7.0)	127 (10.4)	65 (6.4)	86 (6.2)	65 (5.2)	
18.5–23.9	1954 (39.9)	541 (43.9)	430 (42.4)	549 (39.3)	434 (34.7)	

(Continues)

Table 1 (continued)

	Total	Q1 (SBP <117 mmHg)	Q2 (SBP 117–130 mmHg)	Q3 (SBP 131–148 mmHg)	Q4 (SBP >148 mmHg)	P value
≥24	2206 (45.1)	470 (38.1)	445 (43.8)	647 (46.3)	644 (51.5)	
Unmeasured	393 (8.0)	94 (7.6)	75 (7.4)	115 (8.2)	109 (8.7)	
Current smoking	1224 (25.0)	323 (26.2)	252 (24.8)	354 (25.3)	295 (23.6)	0.483
Central laboratory tests						
NT-proBNP (pg/mL)	1487.0 (605.4, 3325.5)	1901.0 (881.0, 3821.0)	1323.0 (565.6, 3212.0)	1369.0 (549.1, 3130.0)	1321.0 (544.2, 3181.0)	<0.001
LDL-C (mmol/L)	2.5 ± 0.9	2.4 ± 0.8	2.5 ± 0.9	2.5 ± 0.9	2.7 ± 0.9	<0.001
Creatinine (µmol/L)	102.4 ± 63.2	94.9 ± 39.6	96.3 ± 53.0	100.3 ± 57.4	117.2 ± 88.4	<0.001
Medication before admission						
ACEIs/ARBs	1720 (35.2)	434 (35.2)	338 (33.3)	503 (36.0)	445 (35.6)	0.560
β-blockers	2080 (42.5)	617 (50.1)	458 (45.1)	581 (41.6)	424 (33.9)	<0.001
Aldosterone antagonists	1820 (37.2)	681 (55.2)	422 (41.6)	455 (32.6)	262 (20.9)	<0.001
Diuretics	999 (20.4)	370 (30.0)	237 (23.3)	250 (17.9)	142 (11.4)	<0.001
Medication during hospitalization						
ACEIs/ARBs	3288 (67.2)	741 (60.1)	636 (62.7)	967 (69.2)	944 (75.5)	<0.001
β-blockers	3609 (73.7)	949 (77.0)	760 (74.9)	1017 (72.8)	883 (70.5)	0.002
Aldosterone antagonists	4075 (83.2)	1076 (87.3)	855 (84.2)	1163 (83.2)	981 (78.4)	<0.001
Diuretics	4302 (87.9)	1119 (90.8)	885 (87.2)	1224 (87.6)	1074 (85.8)	0.001
Digoxin	1640 (33.5)	546 (44.3)	373 (36.7)	425 (30.4)	296 (23.7)	<0.001
Nitrates	3039 (62.1)	655 (53.1)	600 (59.1)	936 (67.0)	848 (67.7)	<0.001
Self-reported health status						
KCCQ score	44.0 ± 22.8	42.7 ± 22.5	44.5 ± 22.7	43.7 ± 23.1	45.2 ± 22.8	0.038

Abbreviations: ACEIs, angiotensin converting enzyme inhibitors; ARBs, angiotensin receptor blockers; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, heart rate; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; LDL-C, low-density lipoprotein cholesterol; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association; SBP, systolic blood pressure.

Figure 2 Kaplan–Meier plots for all-cause death (A) and heart failure readmission (B) by systolic blood pressure quartiles. This study assessed the association of admission systolic blood pressure with outcomes in patients hospitalized with heart failure. Patients were categorized into quartiles by admission systolic blood pressure (<117, 117–130, 131–148, >148 mmHg) for analysis. During 1 year follow up, patients in the 1st systolic blood pressure quartile had higher event rates of all-cause death and heart failure readmission than those in other systolic blood pressure quartiles.
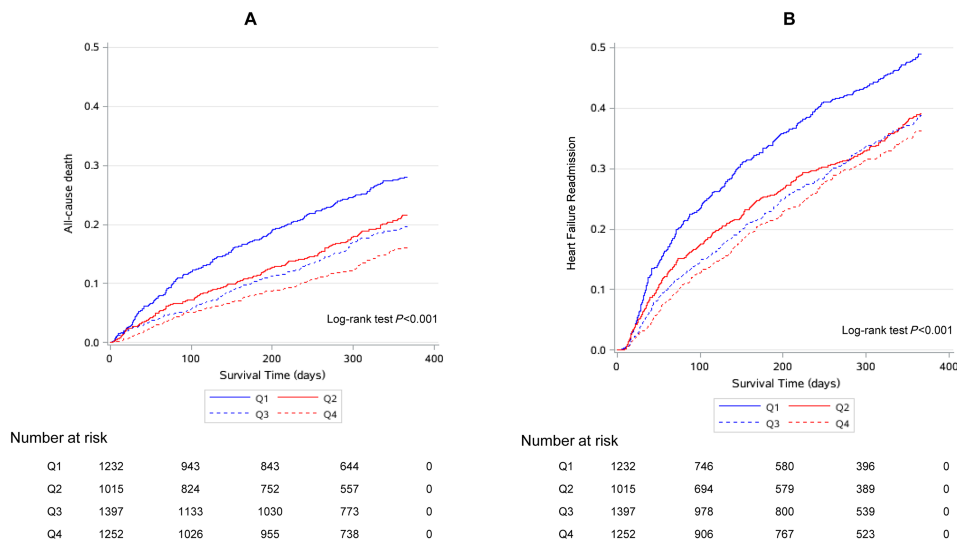
Table 2 Unadjusted and adjusted risk for outcomes according to systolic blood pressure quartiles

	All-cause death		Heart failure readmission	
	Hazard ratio (95% CI)	*p* value	Hazard ratio (95% CI)	*p* value
Unadjusted				
<117 mmHg	1.99 (1.64–2.41)	<0.001	1.61 (1.40–1.85)	<0.001
117–130 mmHg	1.41 (1.14–1.75)	0.001	1.16 (0.99–1.35)	0.062
131–148 mmHg	1.27 (1.03–1.55)	0.022	1.10 (0.95–1.27)	0.188
>148 mmHg	1.00		1.00	
Adjusted for demographic, socio-economic, clinical characteristics, treatment, and self-reported health status				
<117 mmHg	1.85 (1.48–2.33)	<0.001	1.40 (1.19–1.65)	<0.001
117–130 mmHg	1.50 (1.19–1.89)	<0.001	1.09 (0.92–1.29)	0.303
131–148 mmHg	1.30 (1.05–1.60)	0.015	1.04 (0.89–1.20)	0.641
>148 mmHg	1.00		1.00	

Abbreviations: CI, confidence interval.

1st quartile (SBP < 117 mmHg), 293 (23.8%) died compared with 161 (12.9%) of those with SBP in the 4th quartile (SBP > 148 mmHg) ($P < 0.001$). There were 474 (38.4%) patients in the 1st SBP quartile having HF readmission compared with 355 (28.4%) patients in the 4th SBP quartile ($P < 0.001$).

After adjusting covariates, the associations between SBP and 1-year clinical outcomes were slightly attenuated but still significant (*Table 2*). Compared with the 4th SBP quartile, the adjusted hazard ratios (HR) for all-cause death were 1.85 [95% confidence interval (CI) 1.48–2.33; $P < 0.001$] for the 1st SBP quartile, 1.50 (95% CI 1.19–1.89; $P < 0.001$) for the 2nd SBP quartile (SBP of 117–130 mmHg), and 1.30 (95% CI 1.05–1.60; $P = 0.015$) for

the 3rd SBP quartile (SBP of 131–148 mmHg). For HF readmission, patients in the 1st admission SBP quartile were more likely to be readmitted for HF than those in the 4th SBP quartile (adjusted HR, 1.40; 95% CI: 1.19–1.65; $P < 0.001$), and the 2nd and 3rd quartiles had no significant difference in the risk of HF readmission.

Restricted cubic splines for the association between SBP and outcomes were shown in *Figure 3*. Lower admission SBP was associated with significantly higher all-cause death, and this association persisted even at rather high SBP levels. The risk of HF readmission was higher in patients with a lower SBP; however, above a SBP of approximately 120 mmHg, the relationship between SBP and HF readmission got flattened and was not significant.

Figure 3 Restricted spline curve for association between admission systolic blood pressure and all-cause death (A) and heart failure readmission (B). Hazard ratios and 95% confidence intervals for two outcomes by admission systolic blood pressure level in 4896 patients hospitalized with heart failure according to restricted cubic spline regression models using four knots at systolic blood pressures of 97, 121, 140, and 180 mmHg. Solid black lines indicate hazard ratios, and shaded areas indicate 95% confidence intervals.
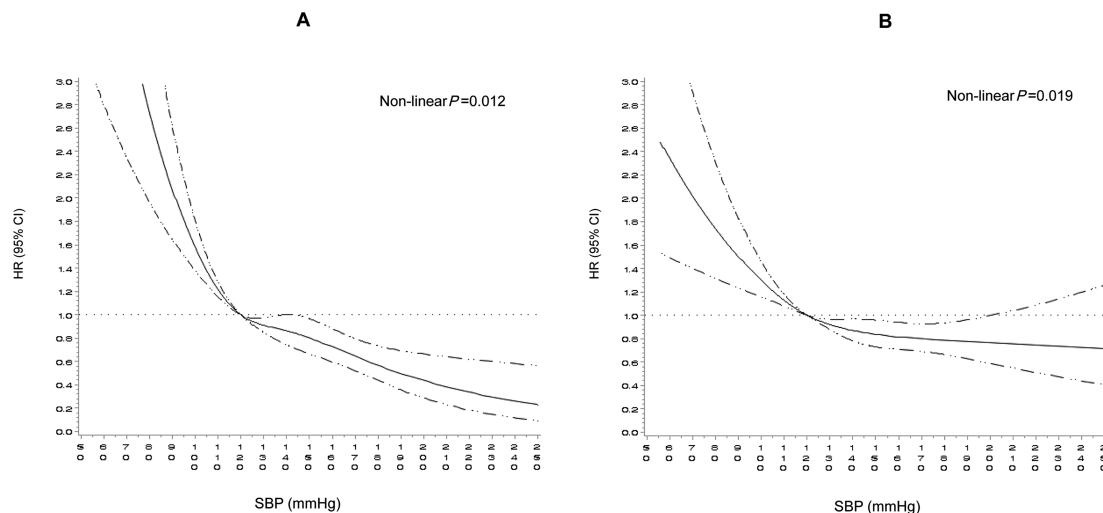
Admission systolic blood pressure and clinical outcomes in subgroups

The association between SBP and all-cause death was consistent across various clinically relevant subgroups of patients, such as age, sex, and LVEF type; although there is an interaction between prescription of aldosterone antagonists and SBP, the directions of the associations in the subgroups were the same (*Figure 4A*). The association between SBP and HF readmission was also consistent across subgroups, except those with diabetes; but the directions were the same (*Figure 4B*).

Discussion

This study demonstrates an independent association between lower admission SBP and higher risk of 1 -year all-cause death in patients hospitalized for the entire spectrum of HF, and there is no threshold; while we only observed such an association with 1 -year HF readmission when admission SBP was lower than 120 mmHg. These associations were consistent across subgroups such as age, sex, LVEF, HF type, and coronary heart disease, and the consistency was not affected by the use of important medications for HF, which have blood pressure-lowering effect, such as ACEIs/ARBs and β-blockers. Our findings could help physicians to stratify the risk of patients hospitalized for HF very early and improve their management of HF patients.

We demonstrate a continuous relationship between lower admission SBP and higher 1 -year death without upper threshold in the whole HF cohort and various subgroups. This

finding is consistent with that in old HF patients, HF patients with reduced ejection fraction, and a Gulf cohort of HF.[8,14,19] Previous studies reported heterogeneous results among subgroups. Barsheshet *et al*. found that among the elderly, the association between SBP and death was inverse linear; in contrast, in patients younger than 75 years, there was a J shape curve.[16] Núñez *et al*. demonstrated that in HF patients with reduced ejection fraction, SBP has an inverse linear relationship with death, while in HF patients with preserved ejection fraction, the relationship showed a J shape curve.[15] The inconsistency may be related to different study populations, sample sizes, and confounders. In this study, we collected comprehensive information on potential confounders in a large cohort. Besides demographic and clinical characteristics, we also adjusted socio-economic status and self-reported health status and the association between low SBP and high risks of 1 -year death persisted without upper threshold. Our findings indicate that SBP measurement at admission for HF patients can help to identify the patients at high risk of 1 year death at a very early time, and to provide intensive care to HF patients with low admission SBP may improve their long-term survival.

This study for the first time shows that lower admission SBP is only associated with increased HF readmission in the range of 117 mmHg and below. HF readmission very frequently occurred after a hospitalization for HF[17,20]; patients with admission SBP below 120 mmHg should be particularly given more attention and more aggressive care to reduce their risk of HF readmission. The association between admission SBP and HF readmission is similar to, but weaker than, that between admission SBP and all-cause death. Compared with the 4th SBP quartile, the 2nd and 3rd quartiles show

Figure 4 Forest plots for subgroup analyses of all-cause death (A) and heart failure readmission (B) by systolic blood pressure quartiles. Forest plots displaying hazard ratios and 95% confidence intervals for all-cause death and heart failure readmission in subgroups of patients hospitalized with heart failure by the 1st systolic blood pressure quartile vs. 4th systolic blood pressure quartile. Abbreviation: ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor blockers; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide.
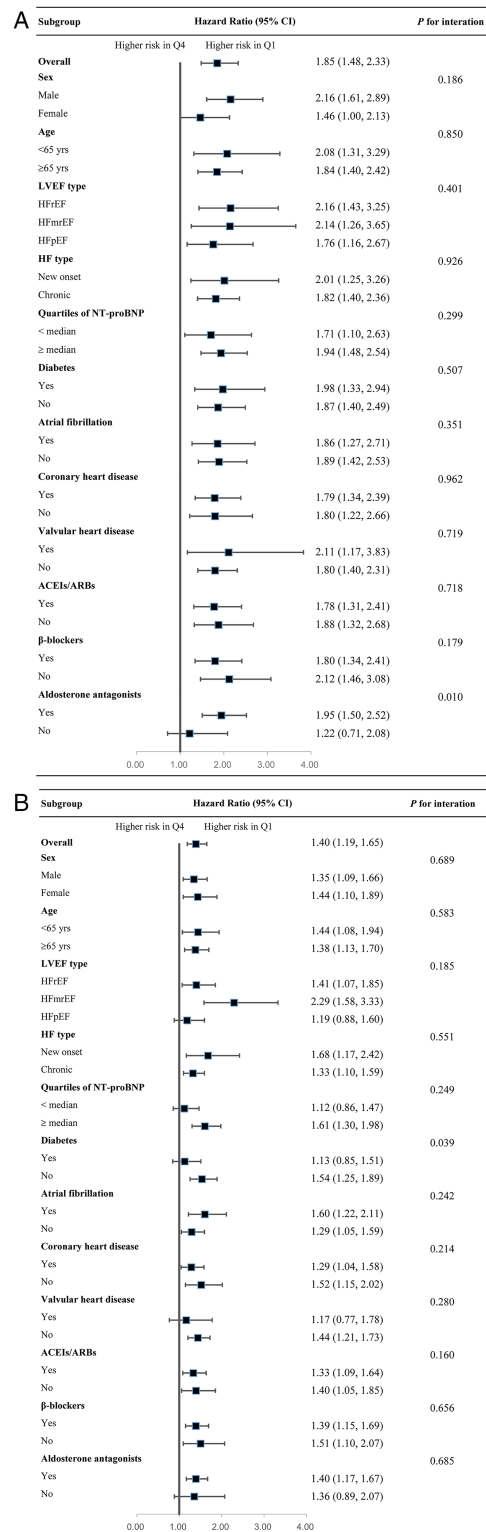
weak but not significant tendencies towards higher risk of HF readmission. There are two possible explanations for the weak and non-significant associations. First, a more modest relative risk of HF readmission may be due to the substantial competing risk of death, that is, patients in lower SBP quartiles may have less opportunity to be readmitted because of increased mortality.[21] Second, apart from disease severity, other factors (e.g. medical resource accessibility and availability) could influence the occurrence of HF readmission.[22,23] We noted that there was a significant interaction between admission SBP and diabetes for HF readmission and no significant association was found between SBP and HF readmission in diabetic patients. These findings may be explained by high rates of HF readmission across all admission SBP quartiles in diabetic patients and the little extra risk added by decreased SBP (*Table S1*).

The association between admission SBP and clinical outcomes remained after adjustment for potential confounders (including demographic and clinical characteristics of patients, proved beneficial medications for HF patients with reduced ejection fraction, socio-economic status, and self-reported health status), although we are uncertain whether the association is causality. Some people argued that patients with lower SBP tend to be older and weaker.[8] However, in this study, old age could not explain the worse prognosis because patients with lower admission SBP were even younger. Although LVEF was lower in patients with lower SBP levels, indicating a worse systolic function,[24,25] the association between admission SBP and death remained significant after adjustment for LVEF. The differences in comorbidities may explain the results,[11] which is however unlikely because patients with higher SBP also have high proportion of comorbidities; even after adjustment for these comorbidities, the associations persisted. In terms of medications, some people stated that physicians may be reluctant to use ACEIs/ARBs or β-blockers in HF patients with lower SBP and tend to treat those with higher SBP more aggressively[26]; however, this study found that even in the lowest SBP quartile, most patients used these medications during hospitalization.

The results should be interpreted in the context of limitations. First, patients with different admission SBP may receive different medications during follow up, but we did not collect comprehensive data about the follow-up medications, which could be confounders. Second, although we minimized the risk of confounding by a thorough multivariate adjustment, other unknown confounders could have been missed, which is inevitable for observational studies.

In conclusion, lower admission SBP was significantly associated with higher risk of all-cause death and there is no threshold, while such an association with HF readmission was only observed when admission SBP was lower than 120 mmHg. These associations were consistent among various clinically important subgroups. These findings can improve risk stratification at very early stage and facilitate more effective management strategies for patients hospitalized for HF.

Conflict of interest

Dr Li reported receiving research grants, through Fuwai Hospital, from the People's Republic of China for work to improve the management of hypertension and blood lipids and to improve care quality and patient outcomes of cardiovascular disease; receiving research agreements, through the National Center for Cardiovascular Diseases and Fuwai Hospital, from Amgen for a multicentre clinical trial assessing the efficacy and safety of omecamtiv mecarbil and for dyslipidaemic patient registration; receiving a research agreement, through Fuwai Hospital, from Sanofi for a multicentre clinical trial on the effects of sotagliflozin; receiving a research agreement, through Fuwai Hospital, with the University of Oxford for a multicentre clinical trial of empagliflozin; receiving a research agreement, through the National Center for Cardiovascular Diseases, from AstraZeneca for clinical research methods training outside the submitted work; and receiving a research agreement, through the National Center for Cardiovascular Diseases, from Lilly for physician training outside the submitted work.

Supporting information

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

Table S1. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for one-year heart failure readmission for systolic blood pressure in diabetic and non-diabetic patients.

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