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Association Between Admission Systolic Blood Pressure and Cardiovascular Events in Acute Myocardial Infarction Patients with Different Left Ventricular Ejection Fractions

ABSTRACT

Background: Among patients with acute heart failure, left ventricular ejection fraction (LVEF) is closely related with admission blood pressure. However, it is unclear whether the systolic blood pressure is associated with the LVEF in acute myocardial infarction (AMI) patients. we evaluated the predictive value of admission SBP in AMI patients with different LVEF status.

Methods: Data were from our hospital database bank. 4114 patients were included in this analysis. Patients were divided into 2 groups according to their LVEF in the first echocardiography record after admission. Patients were categorized into 4 groups (SBP 90-99 mm Hg, SBP 100-119 mm Hg, SBP 120-139 mm Hg, and SBP ≥140 mm Hg) based on SBP level at admission.

Results: The mean age was 64.9 ± 12.5 years and 28% were female. For patients of LVEF < 50% in the lowest SBP group (SBP 90-99 mm Hg), the incidence of in-hospital cardiovascular death was significantly higher than other SBP groups (reference: SBP 90-99 mm Hg) (adjusted OR = 0.267, 95% CI: 0.113-0.728 for SBP 120-139 mm Hg, *P* = .004 and OR = 0.241, 95% CI: 0.089-0.651 for SBP ≥ 140 mm Hg, *P* = .005). Patients of LVEF ≥50% in the highest SBP group (SBP ≥ 140 mm Hg) were at higher risk of cardiogenic mortality during long-term follow-up (reference: SBP ≥140 mm Hg) (adjusted HR = 0.313, 95% CI: 0.489-0.962 for SBP 100-119 mm Hg, *P* < .001, HR = 0.701, 95% CI: 0.488-0.987 for SBP 120-139 mm Hg, *P* = .003, and HR = 0.554, 95% CI: 0.198-0.837 for SBP 90-99 mm Hg, *P* = .001).

Conclusion: SBP 90-99 mm Hg were associated with increased in-hospital cardiovascular death in AMI population with LVEF < 50%, and SBP > 140 mm Hg were associated with increased long-term cardiovascular death in AMI subjects with LVEF >50%.

Keywords: Blood pressure, acute myocardial infarction, left ventricular ejection fractions, cardiovascular events

ORIGINAL INVESTIGATION

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INTRODUCTION

Acute myocardial infarction (AMI) is one of the most severe cardiovascular diseases worldwide.[1-3] Although treatment improvements in AMI patients have been accomplished in the past decades, there were still many puzzles to be solved. Recent evidence indicated that the SBP at admission is one of the most important prognostic factors in patients with acute heart failure, with a higher admission SBP coming along with lower mortality.[4-6] It has been suggested that acute heart failure patients with a higher SBP are more likely to have a normal left ventricular ejection fraction (LVEF), and patients with normal or low SBP tend to have a reduced LVEF.[7] Various risk scores such as the thrombolysis in myocardial infarction (TIMI) risk index included heart rate and systolic blood pressure, demonstrating good predictive value in ST-segment elevated myocardial infarction (STEMI) patients.[8] In AMI patients, systolic dysfunction is an important marker of poor prognosis, so objective measures of LV systolic function are crucial to help determine the best therapies after revascularization.[9,10] However, it is unclear whether the SBP at admission is associated with prognosis in different LVEF statuses (preserved or reduced ejection fraction) in patients with AMI. Therefore, in this study,

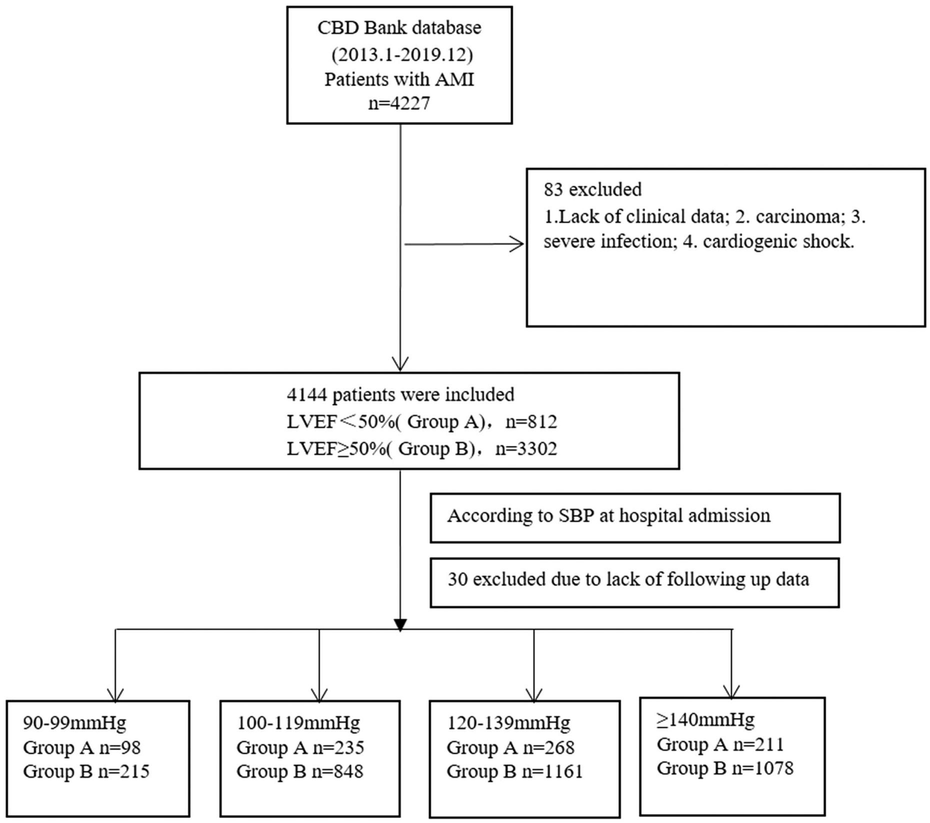

Figure 1. The flowchart of study subject enrollment. AMI, acute myocardial infarction; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure.

we evaluated the predictive value of admission SBP in AMI patients with different LVEF statuses.

METHODS

Study Population

This study is a retrospective, single-center, cohort study including AMI patients that were admitted to the Cardiovascular Center of our hospital between January 2013 and December 2019. The study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of our hospital, with a waiver for informed consent (No. 2017-P2-123-01), and permission was granted to use data for analysis. The included patients met the following criteria: (1) age > 18 years old; (2) diagnosis of acute myocardial infarction according to the Fourth Universal Definition of Myocardial Infarction (2018). Exclusion criteria included: (1) lack of clinical or follow-up data; (2) carcinoma; (3) severe infection; (4) cardiogenic shock, which was defined as dsystolic blood pressure measurements of <90 mm Hg for ≥30 minutes or use of pharmacological and/or mechanical support to maintain an SBP ≥90 mm Hg and evidence of end-organ hypoperfusion (cool extremities or a urine output of <30 ml per hour, and a heart rate of ≥60 beats/min), or a class IV rating according to the Killip classification[11-13]; (5) patients with mechanical complications; (6) patients receiving vasoactive agents to maintain blood pressure. A total of 4227 patients were screened, 83 patients were excluded according to the inclusion and exclusion criteria. Thirty were excluded due to lack of follow-up data. A total of 4114 patients with completed echocardiography within 24-72 hours of admission were finally included for this analysis.

The 4114 patients were divided into 2 groups according to their LVEF from the first echocardiography record after admission: (1) group A: 812 patients with LVEF <50% were divided into 4 groups according to their SBP at hospital admission: SBP 90-99 mm Hg, SBP 100-119 mm Hg, SBP 120-139 mm Hg, SBP ≥140 mm Hg. (2) Group B: 3302 patients with LVEF ≥50% were also divided into 4 groups according to their SBP at hospital admission: SBP 90-99 mm Hg, SBP 100-119 mm Hg, SBP 120-139 mm Hg, SBP ≥140 mm Hg (Figure 1). After discharge, patients were followed up until March 2020. All related data were collected for the following statistical analysis. At the same time, general clinical data of each

HIGHLIGHTS

- For patients of LVEF < 50% in the lowest SBP group (SBP 90-99 mm Hg), the incidence of in-hospital cardiovascular death was significantly higher than other SBP groups.
- For patients of LVEF ≥50% in the highest SBP group (SBP ≥140 mm Hg) were at higher risk of cardiogenic mortality during long-term follow-up.

patient during hospitalization were collected, including baseline data, laboratory indicators, major treatment history, and cardiovascular adverse events that occurred during hospitalization.

In this study, AMI was defined as a typical increase and decrease of cTn values with at least one value above the 99th percentile URL and at least one of the following: (1) symptoms of myocardial ischemia; (2) development of pathological Q waves; (3) new ischemic ECG changes; (4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with ischemic reason; (5) intracoronary thrombosis confirmed by coronary angiography or autopsy.[14] Hypertension was defined as either (1) a previously diagnosed hypertension treated with medication, diet, and/or exercise or (2) SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg on at least 2 occasions. Diabetes was defined as a fasting blood glucose level ≥126 mg/dL (7.0 mmol/L), a non-fasting blood glucose level ≥200 mg/dL (11.1 mmol/L), 75 g oral glucose tolerance test showing a 2-hour blood glucose level ≥200 mg/dL (11.1 mmol/L), HbA1c ≥6.5%, or the patient currently using any anti-diabetes medication. Dyslipidemia was defined as a serum total cholesterol level ≥220 mg/dl (5.72 mmol/L), an LDL-C level ≥140 mg/dL (3.63 mmol/L), triglyceride level ≥150 mg/dL (1.7 mmol/L), or current lipid-lowering therapy.

Blood Pressure Measurements and Clinical Assessment

Admission SBP was measured immediately when patients were admitted to the Cardiology Department (not the emergency room) of our hospital. The physicians measured both upper arms BP after a rest of 5 minutes in the supine position using an automated electronic sphygmomanometer and the higher record was applied in the followed data analysis. Two BP measurements were performed with a 2-minute interval on each patient and the mean BP was recorded and used in the present study. Patients were categorized into 4 groups (SBP 90-99 mm Hg, SBP 100-119 mm Hg, SBP 120-139 mm Hg, SBP ≥ 140 mm Hg) for SBP level on admission.

Baseline laboratory measurements were obtained right after admission. The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation. The CBD Bank collected basic medical information of patients, such as risk factors, cardiovascular disease history, and medication history. Clinical data during hospitalization, including laboratory test results, were collected. Cardiovascular events during hospitalization, based on the patient's medical records, were identified and collected. Clinical data during the follow-up were collected by telephone by trained professionals and recorded in a database. A total of 4114 patients were included in this study. The mean age was 64.9 ± 12.5 years, and 28% were female. The overall mean follow-up duration was 33.2 ± 8.6 months (3-84 months).

Outcomes

The primary outcome was cardiovascular death during hospitalization and during the follow-up period. Secondary outcomes were all-cause death, nonfatal myocardial infarction (MI), malignant arrhythmia, acute stent thrombosis, and stroke during hospitalization.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation as they were normally distributed. Categorical variables are demonstrated as numbers (%). One-way analysis of variance was used to compare different SBP groups if the data were normally distributed, and Kruskal–Wallis H test should be applied if the data were not normally distributed. Chi-square test was used for counting data. Logistic regression and Cox proportional hazard regression models were employed to assess the association between clinical factors and end-point events. The Kaplan–Meier curve method was used to calculate time to clinical end points. Restricted cubic spline (RCS) was used to analyze the relationship between SBP value and all-cause and cardiac mortality. Bonferroni correction was employed for pairwise comparisons and a *P*-value of <.0083 was considered statistically significant due to the 6-time pairwise comparisons among 4 groups. Statistical tests were performed with IBM SPSS statistics 26.

RESULTS

Baseline Characteristics

RCS was employed to investigate the relationship between SBP and all-cause/CV death; it came out that SBP between 115 and 125 mm Hg has a positive impact on the all-cause death (χ^2 = 12.4, P = .004). Similar results were also found in CV death (SBP between 116 and 123 mm Hg) (χ^2 = 13.1 P = .005) (Supplementary Figure 1).

Group A of LVEF < 50% were divided into 4 SBP groups. Patients in the lowest admission SBP group (SBP 90-99 mm Hg) had a significantly higher proportion of STEMI, higher white blood cell count, C-reactive protein, CK-MB peak, and troponin I (TNI) peak levels than the other 3 SBP groups. Patients in the highest admission SBP group (SBP ≥140 mm Hg) were more likely to have a history of hypertension, diabetes, and had higher NT-proBNP level at admission (Table 1).

Group B of LVEF ≥50% was also divided into 4 groups of SBP. Patients in the lowest admission SBP group (SBP 90-99 mm Hg) were younger, more often male, and more smokers, had lower body mass index, and had a higher proportion of STEMI, higher white blood cell count, CK - MB peak, and TNI peak levels. Patients in the highest admission SBP group (SBP ≥140 mm Hg) were more likely to have a history of coronary heart disease, hypertension, diabetes, and had higher NT-proBNP level at admission (Table 1).

We further compared the baseline characteristics between group A and group B (Figure 2). LVEF value in different SBP groups was significantly higher in group B than group A (P = .014, Figure 2A). In all groups, as SBP increased, the proportion of STEMI patients decreased gradually (Figure 2B). Similar results were observed for TNI and CK-MB peak levels (Figure 2C and D). Compared with group B, the levels of NT-proBNP in different admission SBP groups in group A were significantly higher (P = .007, Figure 2E), which is consistent with the poor left ventricular function of the patient in Group A of LVEF < 50%. The level of CRP at admission in group A was higher than that in group B, especially for the group with the lowest SBP (P = .004, Figure 2F), suggesting that the level of

Table 1. Baseline Characteristics of Patients

	Group A, EF < 50%, n = 812					Group B, EF≥ 50%, n = 3302				
	1 Group SBP 90-99 mm Hg, n = 98	2 Group SBP 100-119 mm Hg, n = 235	3 Group SBP 120-139 mm Hg, n = 268	4 Group SBP ≥ 140 mm Hg, n = 211	*P*	1 Group SBP 90-99 mm Hg, n = 215	2 Group SBP 100-119 mm Hg, n = 848	3 Group SBP 120-139 mm Hg, n = 1161	4 Group SBP ≥ 140 mm Hg, n = 1078	*P*
Age, years	66.5 ± 12.5	67.7 ± 11.8	68.3 ± 12.3	70.1 ± 10.9	.069	62.6 ± 11.6	62.4 ± 10.7	63.8 ± 12.1	65.7 ± 11.4	.014
Male gender	75 (76.5)	179 (76.2)	195 (72.8)	151 (71.6)	.666	160 (74.4)	647 (76.3)	862 (74.2)	739 (68.6)	.001
BMI, kg/m²	24.3 ± 4.2	24.4 ± 4.1	25.0 ± 5.0	25.2 ± 4.3	.075	25.3 ± 4.3	25.1 ± 4.6	25.6 ± 4.9	25.9 ± 5.0	.001
SBP, mm Hg	94±3.6	110±2.8	128± 3.7	153 ± 5.8	<.001	95 ± 3.8	110 ± 3.5	128 ± 3.9	154 ± 7.3	<.001
DBP, mm Hg	62 ± 2.7	68 ± 4.8	75 ± 4.2	83 ± 5.2	<.001	63 ± 2.6	66 ± 4.6	73 ± 5.1	82 ± 5.4	<.001
Medical history										
Current/ex-smoker	40 (40.8)	102 (43.4)	103 (38.4)	78 (37.0)	.581	114 (53.0)	443 (52.2)	551 (47.5)	413 (38.3)	<.001
HT	46 (46.9)	132 (56.2)	184 (68.7)	169 (80.1)	<.001	93 (43.3)	433 (51.1)	751 (64.7)	862 (80.0)	<.001
DM	26 (26.5)	99 (42.1)	103 (38.4)	92 (43.6)	.041	51 (23.7)	244 (28.8)	366 (31.5)	371 (34.4)	.004
Dyslipidemia	47 (48.0)	95 (40.4)	114 (42.5)	87 (41.2)	.601	97 (45.1)	373 (44.0)	525 (45.2)	479 (44.4)	.941
Stroke	21 (21.5)	47 (20.0)	53 (19.8)	48 (22.7)	.822	24 (11.2)	104 (12.3)	176 (15.2)	211 (19.6)	<.001
CHD	33 (33.7)	84 (35.7)	107 (39.9)	88 (41.7)	.430	46 (21.4)	197 (23.2)	319 (27.5)	319 (29.6)	.013
OMI	19 (19.4)	50 (21.3)	44 (16.4)	44 (20.9)	.522	16 (7.4)	76 (9.0)	136 (11.7)	99 (9.2)	.067
Past PCI	15 (15.3)	35 (14.9)	29 (10.8)	31 (14.7)	.462	18 (8.4)	76 (9.0)	135 (11.6)	100 (9.3)	.106
HF	4 (4.1)	5 (2.1)	8 (3.0)	3 (1.4)	.417	1 (0.5)	6 (0.7)	6 (0.5)	8 (0.7)	.837
Family history of CHD	25 (25.5)	76 (32.3)	66 (24.6)	48 (22.7)	.113	67 (31.2)	274 (32.3)	365 (31.4)	288 (26.7)	.038
Antiplatelet agent	34 (34.7)	73 (45.1)	89 (33.2)	74 (35.1)	.092	51 (23.7)	208 (24.5)	333 (28.7)	305 (27.2)	.093
Initial diagnosis										
STEMI	76 (77.6)	159 (67.7)	143 (53.4)	93 (44.1)	<.001	149 (69.4)	459 (54.1)	540 (46.5)	404 (37.5)	<.001
Laboratory values										
WBC, 10^9/L	10.55 ± 2.2	9.02 ± 2.5	8.26 ± 3.2	8.26 ± 2.9	<.001	9.91 ± 2.5	8.81 ± 2.1	8.25 ± 2.6	8.08 ± 2.4	<.001
CRP, mg/L	39.30 ± 15.6	21.40 ± 11.8	19.26 ± 13.7	22.97 ± 14.9	.001	12.12 ± 8.5	15.22 ± 9.7	14.92 ± 8.9	12.35 ± 9.1	.553
eGFR, mL/min/1.73 m²	73.92 ± 26.8	83.39 ± 24.7	80.80 ± 27.2	76.42 ± 28.4	.491	88.53 ± 28.9	91.63 ± 27.6	88.95 ± 25.3	78.87 ± 27.9	<.001
HbA1c, %	6.60 ± 2.5	6.72 ± 3.0	6.79 ± 3.2	6.69 ± 3.5	.772	6.39 ± 2.7	6.42 ± 3.2	6.51 ± 3.5	6.62 ± 3.8	.028
TC, mmol/L	4.26 ± 1.4	4.23 ± 1.5	4.31 ± 1.3	4.41 ± 1.7	.332	4.33 ± 1.5	4.43 ± 1.8	4.46 ± 1.7	4.50 ± 1.6	.144
TG, mmol/L	1.32 ± 0.5	1.39 ± 0.7	1.43 ± 0.9	1.53 ± 0.8	.186	1.70 ± 0.6	1.73 ± 0.8	1.77 ± 0.9	1.84 ± 0.7	.272
HDL-C, mmol/L	1.06 ± 0.6	1.04 ± 0.4	1.03 ± 0.7	1.05 ± 0.6	.791	1.02 ± 0.5	1.03 ± 0.8	1.05 ± 0.6	1.06 ± 0.7	.112
LDL-C, mmol/L	2.48 ± 1.3	2.45 ± 1.6	2.51 ± 1.5	2.58 ± 1.8	.345	2.52 ± 1.4	2.58 ± 1.7	2.59 ± 1.6	2.62 ± 1.8	.377
NT-pro BNP	6848 ± 1458	6502 ± 1386	7401 ± 1478	8361 ± 1502	.027	2019 ± 723	1701 ± 689	1976 ± 704	2747 ± 653	<.001
pNT-pro BNP	11 577 ± 2358	10 291 ± 2147	10 113 ± 1988	11 083 ± 2096	.551	4387 ± 1058	3137 ± 984	3107 ± 987	3958 ± 1023	<.001
pCK-MB, ng/mL	190 ± 52	147 ± 49	119 ± 42	93 ± 39	<.001	196 ± 47	116 ± 37	89 ± 36	81 ± 40	<.001
pTNI, ng/ml	24.91 ± 11.2	18.45 ± 9.4	12.91 ± 9.1	11.82 ± 8.9	<.001	22.07 ± 10.8	12.58 ± 9.3	9.35 ± 9.5	9.89 ± 8.7	<.001
Echocardiography										
LA, cm	3.90 ± 1.6	3.99 ± 1.5	4.07 ± 1.7	4.09 ± 1.8	.027	3.71 ± 1.4	3.66 ± 1.6	3.73 ± 1.5	3.79 ± 1.7	.002
LVEDD, cm	5.64 ± 2.0	5.87 ± 1.9	5.91 ± 2.1	5.89 ± 2.2	.031	5.04 ± 1.8	5.06 ± 2.0	5.09 ± 1.9	5.11 ± 2.1	.049
EF	0.42 ± 0.13	0.40 ± 0.16	0.40 ± 0.15	0.41 ± 0.16	.395	0.60 ± 0.18	0.61 ± 0.19	0.62 ± 0.20	0.62 ± 0.17	.360
In-hospital treatment										
PCI	68 (69.4)	158 (67.2)	173 (64.6)	127 (60.2)	.332	185 (86.0)	684 (80.7)	919 (79.2)	796 (73.8)	<.001

Data are presented as mean ± SD or n (%). 1 group: SBP 90-99 mm Hg, 2 group: SBP 100-119 mm Hg, 3 group: SBP 120-139 mm Hg, 4 group: SBP ≥140 mm Hg.
BMI, body mass index; CHD coronary heart disease; Cr, creatinine; CRP, c-reactive protein; DBP, diastolic blood pressure; DM, diabetes mellitus; EDD, end-diastolic diameter; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; HF, heart failure, WBC white blood cell; HT, hypertension; LA, left atrium; LDL-C, low-density lipoprotein cholesterol; LVEDD, left ventricular end-diastolic diameter; OMI, old myocardial infarction; PCI, percutaneous coronary intervention; pCK-MB, the peak value of creatine kinase MB; pNT-proBNP, the peak value of N-terminal pro-brain natriuretic peptide; pTNI, the peak value of troponin I; SBP, systolic blood pressure; TC, total cholesterol, TG triglycerides.

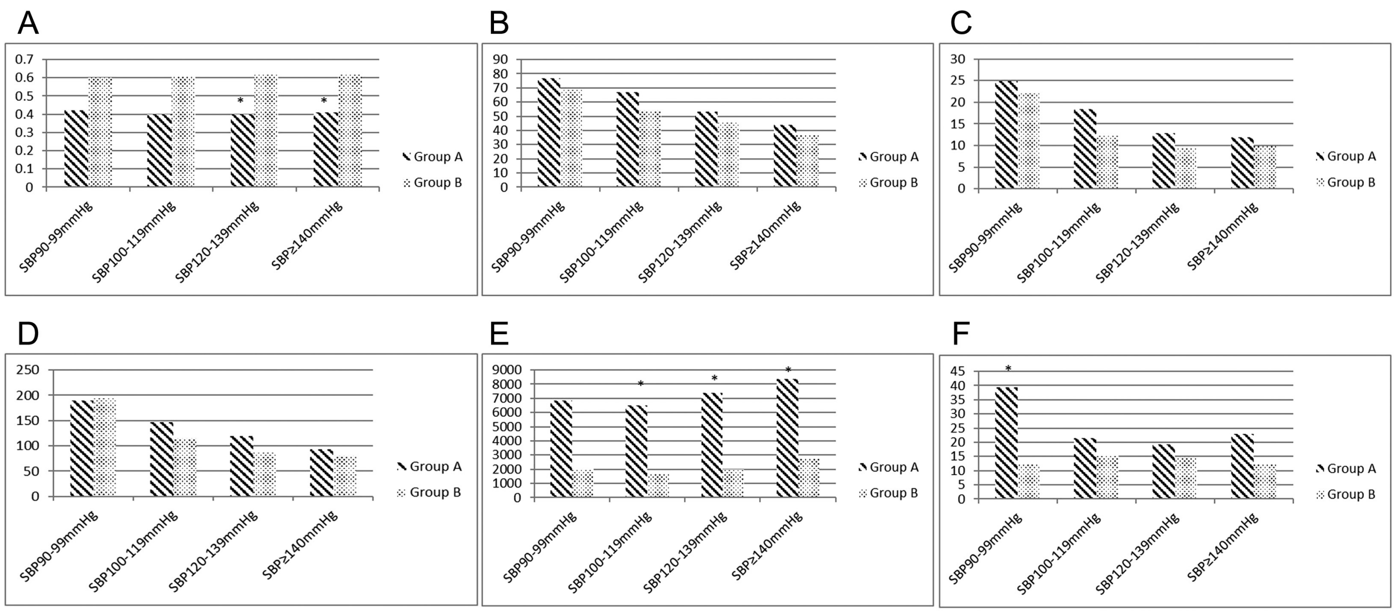

Figure 2. Baseline characteristics and laboratory test results of patients. A: Left ventricular ejection fraction (LVEF); B: Percentage of STEMI; C: pTNI; D: pCK-MB; E: NT-proBNP; F: CRP. pCK-MB, the peak value of creatine kinase MB; pTNI, the peak value of troponin I, group A: LVEF<50%, group B: LVEF ≥50% (P* < .05 compared to group B).**

inflammatory response in patients with AMI complicated with heart failure might be high.

Blood Pressure Outcome Associations

For group A of LVEF <50%, in the lowest SBP group (SBP 90-99 mm Hg), the incidence of cardiovascular death was 14.3%, and the incidence of major adverse cardiac and cerebral events (MACCEs) during hospitalization was 19.45%, and both of these incidence rates were significantly higher than those in the other systolic blood pressure groups (*P*=0.001; see Table 2). However, long-term follow-up results of the patients in this group have shown that there was no significant difference in the incidence of cardiovascular death and all-cause death among the 4 systolic blood pressure groups (Table 2).

For group B of LVEF ≥ 50%, there was no significant difference in the incidence of either cardiovascular death or MACCEs during hospitalization in the 4 different SBP groups (*P*=.001 and *P*=.001, respectively, Table 2). Patients in the highest group of admission SBP (SBP ≥140 mm Hg) had significantly higher rates of cardiovascular death (9.8%) and all-cause death (12.4%) than patients in other SBP groups during long-term follow-up (*P*=.004, and *P*=.002, respectively, Table 2).

Compared with patients with LVEF ≥50%, patients with LVEF <50% had significantly increased cardiogenic mortality during hospitalization and during long-term follow-up (Figure 3). Especially in the LVEF < 50% group, the incidence of MACCEs and cardiovascular death during hospitalization was significantly increased in patients with SBP < 120 mm Hg (*P* < .001, Figure 3A and B). The long-term follow-up results have shown that in all 4 groups, patients with AMI in the LVEF <50% group had poorer long-term outcomes than patients with normal cardiac function (*P* < .001, Figure 3C and 3D).

Patients in the lowest levels of SBP (SBP 90-99 mm Hg, reference category) had significantly higher rates of

Table 2. In-Hospital and Follow-Up Outcomes of Patients

	Group A, EF <50%, n=812					Group B, EF ≥50%, n=3302				
	1 group, n=98	**2 group, n=235**	**3 group, n=268**	**4 group, n=211**	***P***	**1 group, n=215**	**2 group, n=848**	**3 group, n=1161**	**4 group, n=1078**	***P***
In-hospital outcomes										
Composite MACCEs	19 (19.5)	33 (14.0)	18 (6.7)	16 (7.6)	.001	14 (6.5)	43 (5.1)	53 (4.6)	34 (3.2)	.003
CV death	14 (14.3)	24 (10.2)	12 (4.5)	9 (4.3)	.001	5 (2.3)	13 (1.5)	18 (1.6)	12 (1.1)	.513
Follow-up outcomes										
All-cause death	29 (29.6)	61 (26.0)	67 (25.0)	63 (29.9)	.359	20 (9.3)	67 (7.9)	106 (9.1)	134 (12.4)	.004
CV death	27 (27.6)	58 (24.7)	61 (22.8)	49 (23.2)	.328	16 (7.4)	52 (6.1)	80 (6.9)	106 (9.8)	.002

Values are presented as numbers (%). Composite MACCEs include: all-cause death, nonfatal MI, malignant arrhythmia, acute stent thrombosis, and stroke. Group 1: SBP 90-99 mm Hg, Group 2: SBP 100-119 mm Hg, Group 3: SBP 120-139 mm Hg, Group 4: SBP ≥ 140 mm Hg.CV, cardiovascular; MACCEs, major adverse cardiac and cerebral events.

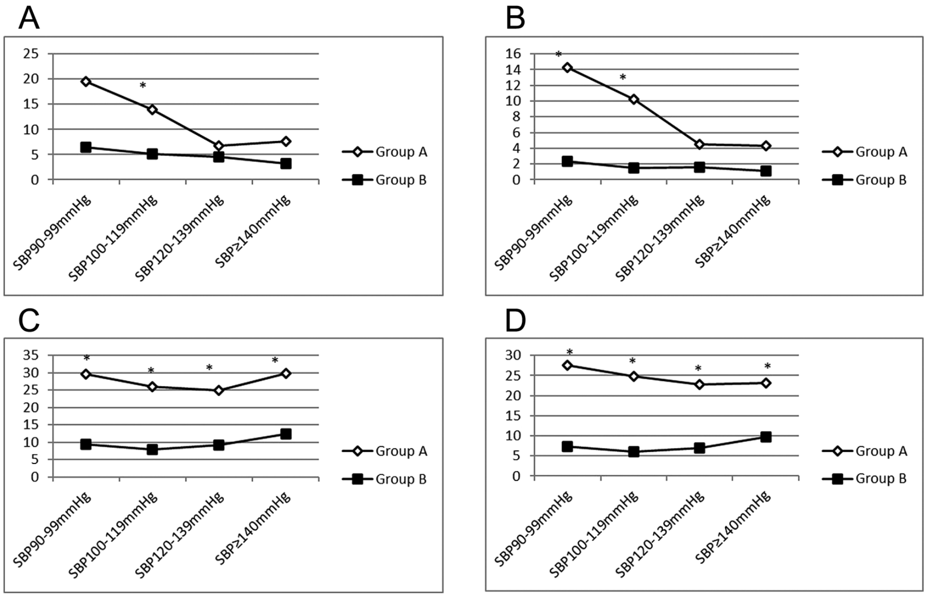

Figure 3. Comparison of in-hospital and follow-up outcomes of the 4 SBP groups. A: MACCEs during hospitalization; B: cardiogenic death during hospitalization; C: all-cause death during follow-up; D: cardiogenic death during follow-up. Composite MACCEs include: all-cause death, non-fatal MI, malignant arrhythmia, acute stent thrombosis, and stroke. (*P < .05 compared to the group B).

cardiovascular death compared to patients with SBP 120-139 mm Hg (adjusted OR = 0.267, 95% CI: 0.113-0.728, P = .004) and patients with SBP ≥140 mm Hg (adjusted OR = 0.241, 95% CI: 0.089-0.651, P = .005). Compared with SBP 90-99 mm Hg patients, the risk of cardiovascular death in SBP 100-119 mm Hg group showed a trend of reduction (adjusted OR = 0.791, 95% CI 0.324-1.803, P = .602), and consistent findings were also observed for major adverse cardiac and cerebral events in the SBP 100-119 mm Hg group (Table 3). Multiple logistic regression analysis indicated that three clinical factors including age, renal function, and heart failure are closely related with cardiovascular death (Table 3). In addition, age, heart failure, and previous myocardial infarction were associated with composite MACCEs during hospitalization.

The patients of LVEF ≥50% in the highest SBP group (SBP ≥140 mm Hg) were at significantly higher risk of cardiovascular death during long-term follow-up. Patients in the highest levels of SBP (SBP ≥140 mm Hg, reference category) presented a significantly increased risk of cardiovascular death [adjusted HR = 0.313, 95% CI: 0.489-0.962 for SBP 100-119 mm Hg, P < .001, HR = 0.701, 95% CI: 0.488-0.987 for SBP 120-139 mm Hg, P = .003, and HR = 0.554, 95% CI: 0.198-0.837 for SBP 90-99 mm Hg, P = .001] (Table 4). Renal function, smoking history, history of hypertension and heart failure, and the usage of beta-blockers were associated with cardiovascular death in the following up period (Table 4). The survival curve showing the effect of different SBP on mortality adjusted to other prognostic factors is presented in Figure 4.

DISCUSSION

The results of this study revealed that SBP 90-99 mm Hg was associated with increased in-hospital cardiovascular death in systolic dysfunction population of AMI, and SBP > 140 mm Hg was associated with increased long-term cardiovascular death in normal left ventricular systolic function population of AMI.

In our study, patients with low admission SBP and LVEF <50% also had high proportion of STEMI, with high white blood cell count, CRP, CK-MB peak, and TNI peak levels, suggesting that the level of inflammatory response in patients with AMI complicated with heart failure might be high. All these variables at high levels have been found to be associated with poor outcomes in patients with heart failure and/or MI.[15,16] In the group of LVEF <50%, NT-proBNP levels increased as BP increased, suggesting that in addition to heart failure factors, the increase in ventricular wall pressure caused by elevated blood pressure might also be a cause. TNI and CK-MB are biomarkers of myocardial necrosis. As SBP increases, the peak levels of TNI and CK-MB in patients gradually decreased, suggesting that the low SBP in patients with AMI, whether accompanied by heart failure, may be related to the extensive area and severity of myocardial necrosis. In group A (LVEF < 50%) of this study, after adjustment with potential confounders, SBP 90-99 mm Hg was associated with cardiogenic death and major composite end point events during hospitalization, suggesting that low SBP is an unsatisfactory hemodynamic condition when associated with low cardiac output. Interestingly, in the group A (LVEF < 50%), SBP ≥140 mm Hg was not associated with short-term or long-term cardiovascular outcomes; patients with AMI complicated with heart failure and with admission SBP < 120 mm Hg could have poor short-term outcomes. These findings may support the theory that higher blood pressure is required to maintain coronary perfusion during the

Table 3. Multiple Logistic Regression Analysis of Cardiovascular Death and MACCEs in Hospital (Group A)

SBP Groups	Crude OR (95% CI)	*P*	Adjusted OR[a] (95% CI)	*P*
Cardiovascular death				
90-99 mm Hg	1	–	1	–
100-119 mm Hg	0.674 (0.327-1.304)	.234	0.791 (0.324-1.803)	.602
120-139 mm Hg	0.285 (0.115-0.622)	<.001	0.267 (0.113-0.728)	.004
≥140 mm Hg	0.267 (0.111-0.641)	<.001	0.241 (0.089-0.651)	.005
Age	1.035 (1.017-1.061)	<.001	1.034 (1.004-1.078)	.001
BMI	0.918 (0.804-0.998)	.052	-	.426
EGFR	0.981 (0.942-0.994)	<.001	0.973 (0.962-0.997)	.002
Smoking	0.431 (0.201-0.780)	.005	-	.353
Hypertension	1.335 (0.713-2.377)	.306		
Diabetes	1.433 (0.802-2.355)	.186		
Heart failure	7.264 (2.931-20.133)	<.001	6.709(1.966-21.914)	<.001
Previous myocardial infarction	1.196 (0.619-2.281)	.543		
PCI	1.112 (0.584-1.955)	.437		
Previous stroke	1.913(1.188-3.354)	.023	-	.106
Peripheral artery disease	2.021(0.866-4.672)	.101		
The peak value of TNI	1.108 (0.989-1.021)	.233		
Composite MACCEs				
90-99 mm Hg	1	-	1	-
100-119 mm Hg	0.665 (0.321-1.233)	.211	0.718 (0.345-1.511)	.444
120-139 mm Hg	0.256 (0.143-0.534)	.001	0.301 (0.122-0.677)	.001
≥140 mm Hg	0.332 (0.118-0.782)	<.001	0.311 (0.146-0839)	<.001
Age	1.033 (1.011-1.044)	<.001	1.027 (1.001-1.032)	<.001
BMI	0.952 (0.881-1.045)	.108		
EGFR	0.977 (0.956-0.991)	<.001	0.912(0.886-0.979)	.005
Smoking	0.611 (0.377-1.018)	.034		
Hypertension	1.254 (0.568-1.886)	.244		
Diabetes	1.121 (0.633-1.656)	.772		
Heart failure	4.34 (1.677-2.211)	<.001	3.117 (1.012-8.126)	.003
Previous myocardial infarction	2.123 (1.449-4.114)	<.001	2.322 (1.307-3.438)	.001
PCI	1.019 (0.843-1.574)	.078		
Previous stroke	1.414 (0.750-2.386)	.122		
Peripheral artery disease	1.501 (0.693-3.339)	.303		
The peak value of TNI	1.112 (0.976-1.154)	.436		

[a]Models adjusted for age, body mass index, estimated glomerular filtration rate, smoking status, history of hypertension, diabetes, heart failure history, previous myocardial infarction, previous stroke, peripheral artery disease, and the peak value of troponin I. Group A: EF <50%.
CV, cardiovascular; MACCEs, major adverse cardiac and cerebral events; MI, myocardial infarction; PCI, percutaneous coronary intervention.

acute phase of AMI in patients with combined heart failure influencing cardiac output or vascular tone.[5,17,18] Our results indicated that heart failure is closely related to both cardiovascular death and MACCEs, which was supported by previous evidence that patients with lower admission systolic blood pressure were more likely to have a reduced ejection fraction. While SBP ≥ 140 mm Hg was associated with poor long-term prognosis in AMI patients with LVEF ≥ 50%. One possible explanation is that it is not hypotension that causes adverse outcomes, but that the "sicker" patients have lower blood pressure.[19,20] The Systolic Blood Pressure Intervention trial (SPRINT) also indicated that the intensive treatment benefit was observed regardless of the presence of previous cardiovascular diseases.[21] However, the SPRINT trial included patients with fewer rates of heart failure and previous cardiovascular complications (<20%). Another study found that lower average systolic blood pressure led to more severe MI injury.[22] These findings indicated that there may be a complicated relationship in this situation. Further study found a "U curve phenomenon" between blood pressure and Major Adverse Cardiac and Cerebral Events (MAACE) rate in patients with AMI.[23] In Tables 3 and 4, we found that heart failure is an important clinical factor related to clinical outcomes both in the hospital and follow-up period. In

Table 4. Multiple Cox Regression Analysis of Cardiovascular Death in Follow-Up (Group B)

SBP Groups	Crude OR (95% CI)	*P*	Adjusted OR[a] (95% CI)	*P*
Cardiovascular death				
90-99 mm Hg	0.512 (0.215-1.234)	.007	0.554 (0.198-0.837)	.001
100-119 mm Hg	0.633 (0.432-0.877)	<.001	0.313 (0.489-0.962)	<.001
120-139 mm Hg	0.622 (0.537-0.936)	.007	0.701 (0.488-0.987)	.003
≥140 mm Hg	1	-	1	-
BMI	0.785 (0.611-0.997)	.012	0.913 (0.781-0.981)	.004
EGFR	0.977 (0.933-0.982)	<.001	0.986 (0.880-0.995)	<.001
Smoking	0.554 (0.441-0.783)	<.001	1.566 (1.121-2.354)	.001
Hypertension	2.160 (1.320-2.511)	<.001	1.242 (1.035-2.214)	.001
Diabetes	1.436 (1.122-1.929)	<.001	1.184 (0.874-1.559)	.421
Heart failure	10.603 (5.144-20.584)	<.001	3.222 (1.456-7.014)	<.001
Previous myocardial infarction	1.142 (0.564-1.786)	.644		
PCI	1.201 (0.609-1.778)	.423		
Previous stroke	1.622 (1.214-2.043)	.006	1.159 (0.967-1.221)	.350
Peripheral artery disease	1.5 (0.911-2.512)	.143		
The peak value of TNI	0.869 (0.732-1.032)	.203		
ACEI/ARB	0.503 (0.426-0.608)	.011	0.522 (0.434-1.142)	.132
Beta-blocker	0.501 (0.322-0.768)	<.001	0.670 (0.514-0.873)	<.001

[a]Models adjusted for body mass index, estimated glomerular filtration rate, smoking status, history of hypertension, diabetes, heart failure history, previous myocardial infarction, previous stroke, peripheral artery disease, and the peak value of troponin I, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and beta-blockers.
Group B: EF ≥50%. PCI, percutaneous coronary intervention.

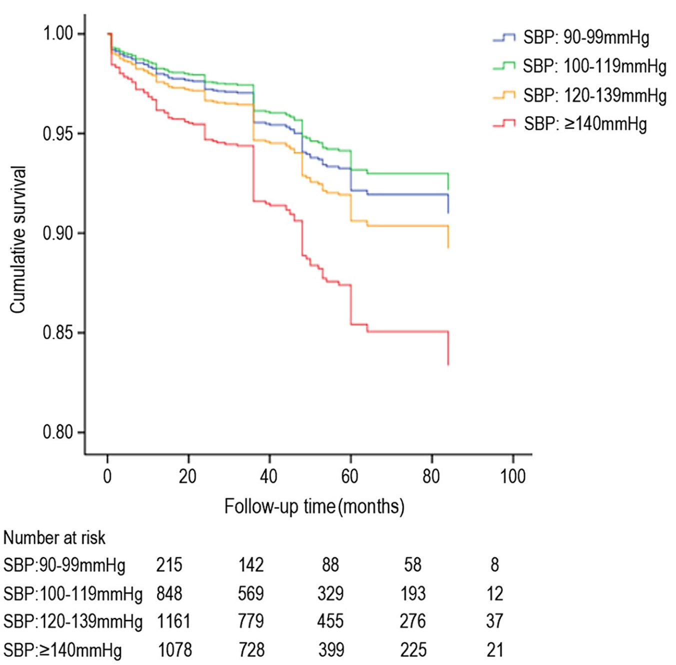

Figure 4. Survival curves free from cardiovascular death during follow-up. Adjusted for age, body mass index, estimated glomerular filtration rate, smoking status, history of hypertension, diabetes, heart failure history, previous myocardial infarction, previous stroke, peripheral artery disease, and the peak value of troponin I, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and beta-blockers.

addition, the SPRINT study did not include patients with acute myocardial infarction, so the intensive blood pressure control strategies may not be applied to acute myocardial infarction patients. Our data demonstrated that there was a complicated relationship between admission systolic blood pressure and ejection fraction in AMI patients. Proper blood pressure control should consider admission blood pressure and ejection fraction.

In a post hoc analysis derived from the Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial (ONTARGET)[24] and the Telmisartan Randomized Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease (TRANSCEND),[25] the authors found a "'J-shaped association" of SBP with clinical outcomes. These results suggest that different blood pressure targets should be used for different populations. Combining with our findings, it suggests that in patients with acute myocardial infarction, blood-control strategies should be very cautious in patients with LVEF<50%. While for those with LVEF>50%, patients may benefit from intensive blood pressure control.

It was recently reported that early echocardiography could provide useful diagnostic and therapeutic information, indicating that all AMI patients should be evaluated as soon as possible to determine the treatment strategies.[26,27] Previous evidence from our group found a "J-curve" relationship between admission SBP and cardiovascular mortality,[28] but we further noted that the relationship between admission SBP and outcomes was also varied for different cardiac functional statuses. So, the evaluations of functional and structural changes in AMI patients should include both the admission SBP and assessment of LVEF. Once aware of this knowledge, antihypertensive strategies will be carried out carefully in AMI patients, especially for those with ventricular dysfunction. For patients with ventricular dysfunction, it would be advisable to take cautious measures, and more positive strategies may be recommended in patients with normal ventricular function.

Study Limitations

Several limitations of this study should be acknowledged: (1) This is a retrospective study of AMI populations in which hypertension history (although more than half of the patients were hypertensive) was not an entry criterion, hence the results presented herein cannot be extrapolated to other populations; (2) despite extensive adjustment, many unmeasured variables (such as the time of admission of the patients to the hospital and the timing of the angiographic intervention) could cause residual confounding bias; (3) the short follow-up time for cardiovascular events in some patients may affect the correlation described in this study; (4) medication dosage or changes during follow-up are not available in the dataset, therefore, we cannot ascertain which patients had treatment intensification during the trial.

CONCLUSION

The present study on a selected population of AMI patients with different LVEF found that SBP 90-99 mm Hg was associated with poor cardiovascular outcomes during hospitalization in systolic dysfunction population, and that SBP ≥140 mm Hg was associated with worse cardiovascular outcomes during long-term outcomes in normal left ventricular systolic function population.

Availability of data and materials: The datasets generated and/or analyzed during the current study are not publicly available due to the provisions of the CBD Bank but are available from the corresponding author on reasonable request.

Ethics Committee Approval: The study data collection was approved by the Institutional Review Board of Beijing Friendship Hospital affiliated to Capital Medical University.

Informed Consent: Written informed consent was obtained from all patients. All methods were performed in accordance with the relevant guidelines.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – H.C.; Design – H.L., H.C.; Supervision – H.C.; Resources – H.L.; Materials – Y.X., Y.Z.; Data Collection and/or Processing – M.W., W.L., H.Q.; Analysis and/or Interpretation – Y.Z.; Literature Search – Y.Z.; Writing – H.Q.; Critical Review – Y.X., W.L.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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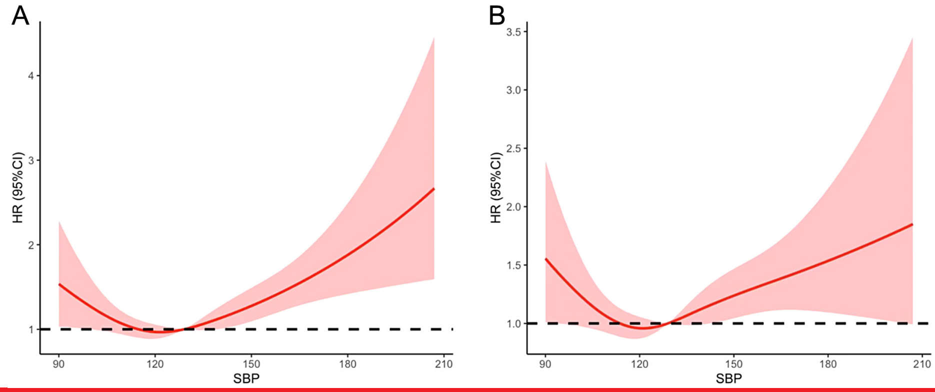

Supplementary Figure 1. Restricted cubic spline analysis for association of SBP and 1-year all-cause (A) and cardiac mortality (B). SBP, systolic blood pressure