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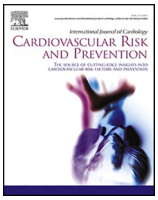

Effect of different blood pressure levels on short-term outcomes in hospitalized heart failure patients☆

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ABSTRACT

Background: To investigate the influence of blood pressure (BP) level on short-term prognosis of heart failure (HF), the effect of the BP level on clinical end point events 3 months after discharge was observed.
Methods: A retrospective cohort study was performed on 1492 hospitalized HF patients. All patients were divided according to systolic blood pressure (SBP) per 20 mmHg and diastolic blood pressure (DBP) per 10 mmHg. Logistic regression analysis was used to analyze the relationship between BP level and heart failure rehospitalization, cardiac death, all-cause death and a composite end point of heart failure rehospitalization/all-cause death at 3 month follow-up after discharge.
Results: After multivariable adjustment, the relationship between SBP and DBP levels and outcomes followed an inverted J curve relationship. Compared with the reference group (110 < SBP≤130 mmHg), the risk of all end point events significantly increased in the SBP≤90 mmHg group included heart failure rehospitalization (*OR* 8.16, *95%CI* 2.88–23.11, $P < 0.001$), cardiac death (*OR* 5.43, *95%CI* 1.97–14.96, $P = 0.001$), all-cause death (*OR* 4.85, *95%CI* 1.76–13.36, $P = 0.002$), and composite end point (*OR* 2.76, *95%CI* 1.03–7.41, $P = 0.044$). SBP>150 mmHg significantly increased the risk of heart failure rehospitalization (*OR* 2.67, *95%CI* 1.15–6.18, $P = 0.022$). Compared with.
the reference group (65 < DBP≤75 mmHg), cardiac death (*OR* 2.64, *95%CI* 1.15–6.05, $P = 0.022$) and all-cause death (*OR* 2.67, *95%CI* 1.20–5.93, $P = 0.016$) was significantly increased in DBP≤55 mmHg group. There was no significant difference among subgroups according to left ventricular ejection fraction ($P > 0.05$).
Conclusions: There is a significant difference in the short-term prognosis 3 months after discharge in HF patients with different BP levels at discharge. There was an inverted J curve relationship between BP levels and prognosis.

1. Introduction

Heart failure (HF) is the severe and terminal stage of various heart diseases. The mortality of HF is high, and the five-year survival rate is less than 50%, which is similar to that of malignant tumors.[1] HF has become a global major public health problem, how to improve the prognosis is very important.

The relationship between blood pressure (BP) and HF is close and complex. Hypertension is an important risk factor leading to HF, and is the second cause after ischemic heart disease. [2] Prevention and treatment of hypertension can effectively reduce the risk of HF. Moreover, There is also evidence of significant differences in prognosis (cardiovascular events and mortality) for patients with HF with different BP levels.[3–10]However, there are still many controversies and uncertainties regarding the optimal BP target in patients with HF, whether there is a J-shaped or U-shaped curve between BP control and prognosis, and how to manage BP in patients with HF. There is still a lack of adequate evidence-based BP management programs [11].

The purpose of this study was to observe whether there were differences in the effects of different BP levels on the clinical endpoint events 3 months after discharge in patients with HF, so as to explore the effects of BP levels on the short-term prognosis of patients with HF, and to provide a possible basis for the formulation of BP control programs for patients with HF.

☆ The manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work, if that information is not provided in another form.

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2. Materials and methods

2.1. Study population

This study was a retrospective cohort study. The study population was collected from Tianjin Medical University General Hospital and Tianjin Chest Hospital, which are the largest general hospital and the largest cardiovascular disease specialized hospital in Tianjin respectively, and theses hospitals can better reflect the diagnosis and treatment level of cardiovascular diseases in Tianjin. A total of 1492 hospitalized patients whose main diagnosis was HF and whose clinical data were complete from March 2014 to February 2016 were included. Patients with HF were included according to the criteria for diagnosis and classification of HF in European Guidelines for diagnosis and Treatment of Acute and Chronic Heart Failure (2016) [12] and Chinese Guidelines for Diagnosis and Treatment of Heart Failure (2018) [2]. Deaths during hospitalization were excluded. Approved by the Medical Ethics Committee of Tianjin Medical University General Hospital (Approval No.: IRB2017-029-01).

2.2. Date collection and follow-up

Case data that met inclusion and exclusion criteria were collected from both hospitals through electronic case and medical records department. Our study collected the general information of patients (age, gender, BP), cardiac function related indicators [NYHA classification, brain natriuretic peptide (BNP), N-terminal pro-brain natriuretic peptide (NT-proBNP), left ventricular ejection fraction (LVEF)], etiology and complications [coronary heart disease, hypertension, cerebrovascular disease, atrial fibrillation, type 2 diabetes, chronic kidney dysfunction (CKD)], and drug therapy [angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), β blockers, calcium channel blockers (CCBs), mineralocorticoid receptor antagonist (MRA)]. Patients were followed up 3 months after discharge, and the incidence of outcomes, including heart failure rehospitalization, all-cause death, and cardiac death, was recorded. The follow-up was carried out by telephone and medical records for re-hospitalization.

2.3. BP stratification

The BP in this study was the discharge BP, which refers to the BP measured within 2 days before discharge. If the patient had two or more BP measurements within 2 days before discharge, the mean value of BP measurements was taken as discharge BP. Systolic blood pressure (SBP) was stratified every 20 mmHg and divided into 5 groups: SBP≤90 mmHg (n = 28), 90 < SBP≤110 mmHg (n = 353), 110 < SBP≤130 mmHg (n = 728), 130 < SBP≤150 mmHg (n = 315) and SBP>150 mmHg (n = 68); Diastolic blood pressure (DBP) was stratified according to every 10 mmHg and divided into 5 groups: DBP≤55 mmHg (n = 65), 55 < DBP≤65 mmHg (n = 356), 65 < DBP≤75 mmHg (n = 575), 75 < DBP≤85 mmHg (n = 408) and DBP>85 mmHg (n = 88).

2.4. Outcomes

For this retrospective analysis, the outcomes were (1) heart failure rehospitalization, (2) all-cause death, (3) cardiac death, and (4) a composite end point of heart failure rehospitalization/all-cause death at 3 month follow-up after discharge.

2.5. Statistical analysis

Baseline data are presented as mean ± SD and medians with quartile 1 and quartile 3 and compared using the chi-square test for categorical data and the Mann-Whitney U and Kruskal–Wallis tests for continuous data. The skewness and kurtosis of continuous variables are calculated to determine whether the continuous variables obey normal distribution. Associations between different levels of SBP and DBP and 3 months of clinical endpoint events were evaluated using logistic regression models. Multivariable models are adjusted for age, sex, comorbidities, medication, cardiac function grading, etc..A univarious analysis was performed to determine the adjusted confounding factors in the multivariate analysis. The SBP group (110 < SBP≤130 mmHg) or DBP group (65 < DBP≤75 mmHg) was used as a reference group and their adjusted odds ratio (OR) was considered 1 and compared to other SBP or DBP groups. A 2-sided P value of <0.05 was considered statistically significant. Analyses were conducted using SPSS Version 22.0.

3. Results

3.1. Flow chart and baseline characteristics

There are 1966 patients in the database, and patients without blood pressure measurements, repeated entries and lost follow-up have been excluded (Supplementary Fig. 1). A total of 1492 patients was enrolled in this study, with an average age of 68.00 ± 12.48 years, including 937 males (62.8%) and 555 females (37.2%). The baseline characteristics of different SBP groups are shown in Table 1. With the increase of SBP, patients tended to be older, with higher LVEF value, higher HFpEF proportion, more complicated with hypertension and CKD, less use of β -blockers, more use of ARBs and CCBs (all $P < 0.05$). The baseline characteristics of different DBP groups were described in Table 2. With the increase of DBP, patients tended to be male, more complicated with hypertension, and type 2 diabetes, more use of ARBs, CCBs (all $P <$ 0.05).

3.2. Associations between BP levels and end point events incidence

During the follow-up period of 3 months after discharge, 84 cases of heart failure rehospitalization, 76 cases of cardiac death, and 95 cases of all-cause death occurred. According to SBP, the 110 < SBP≤130 mmHg group had on the lowest incidence of heart failure rehospitalization and heart failure rehospitalization/all-cause death composite events, while the incidence of these events was significantly increased in the group with the lowest SBP (SBP≤90 mmHg) and the group with the highest SBP (SBP>150 mmHg). For cardiac and all-cause deaths, the event rates in the SBP≤90 mmHg group were significantly higher than those in the other SBP groups. (all $P < 0.05$) (Table 3).

According to DBP, the event rates of cardiac death and all-cause death in DBP≤55 mmHg group were significantly higher than those in other DBP groups (all $P < 0.05$). There were no significant differences in the incidence of heart failure rehospitalization and heart failure rehospitalization/all-cause death composite end point among DBP groups (all $P > 0.05$). (Table 3).

3.3. Associations between BP levels and outcomes

The odds ratios of clinical end point events 3 months after discharge for heart failure patients with different SBP and DBP levels are shown in Table 4, Fig. 1a, and Fig. 1b. The relationship between BP (whether systolic or diastolic) of patients with HF and the risk of endpoint events is non-linear, presenting a reverse J-shaped curve relationship, that is, patients with HF with low BP (SBP≤90 mmHg, DBP≤55 mmHg), the risk of end-point events is significantly increased (Table 4, Fig. 1a and 1b). The confounding factors were determined by univariate analysis (Supplementary Table 1).

According to SBP, all end points in the SBP≤90 mmHg group included heart failure rehospitalization (*OR* 8.16, *95%CI* 2.88–23.11, $P < 0.001$), cardiac death (*OR* 5.43, *95%CI* 1.97–14.96, $P = 0.001$), all-cause death (*OR* 4.85, *95%CI* 1.76–13.36, $P = 0.002$), and heart failure rehospitalization/all-cause death composite endpoint (*OR* 2.76, *95% CI* 1.03–7.41, $P = 0.044$), compared with the reference group (110 < SBP≤130 mmHg). Compared with the reference group (110 < SBP≤130

Table 1
Baseline characteristics of HF patients divided by different systolic blood pressure levels.

	Total n = 1492	SBP≤90 mmHg n = 28	90 < SBP≤110 mmHg n = 353	110 < SBP≤130 mmHg n = 728	130 < SBP≤150 mmHg n = 315	SBP > 150 mmHg n = 68	*P*
Male	937 (62.8)	17 (60.7)	222 (62.9)	470 (64.6)	188 (59.7)	40 (58.8)	0.594
Age	68.00 ± 12.48	64.04 ± 11.99	65.67 ± 12.21	68.66 ± 12.00	68.99 ± 13.07	70.04 ± 14.57	< 0.001
BNP,pg/ml	792.00 (531.75–1422.50)	109 (43-)	703.00 (586.25–1032.50)	681.00 (513.50–1330.00)	842.00 (534.50–1420.00)	1415.00 (622.75–2772.50)	0.015
NT proBNP,pg/ml	2854.00 (1491.50–6889.50)	3545.00 (1539.00–111130.00)	3033.00 (1530.00–6801.00)	2792.00 (1309.00–7002.00)	2773.00 (1547.500–6557.500)	4954.00 (2075.50–17668.25)	0.349
LVEF,%	40.00 (34.00–47.00)	39.00 (32.75–42.75)	39.00 (33.00–45.00)	40.00 (34.00–47.00)	42.00 (35.00–48.00)	42.50 (37.00–55.75)	< 0.001
Causes and comorbidities							
Coronary heart disease	1199 (80.4)	21 (75.0)	274 (77.6)	590 (81.0)	260 (82.5)	54 (79.4)	0.495
Hypertension	878 (58.8)	12 (42.9)	153 (43.3)	426 (58.5)	229 (72.7)	58 (85.3)	< 0.001
Diabetes	474 (31.8)	3 (10.7)	104 (29.5)	218 (29.9)	130 (41.3)	19 (27.9)	< 0.001
Cerebrovascular disease	351 (23.5)	7 (25.0)	70 (19.8)	179 (24.6)	78 (24.8)	17 (25.0)	0.475
Atrial fibrillation	399 (26.7)	8 (28.6)	98 (27.8)	184 (25.3)	94 (29.8)	15 (22.1)	0.502
CKD	274 (18.4)	3 (10.7)	36 (10.2)	111 (15.2)	82 (26.0)	42 (61.8)	< 0.001
Cardiac functional grading							< 0.001
NYHA I	12 (0.8)	1 (3.6)	3 (0.8)	5 (0.7)	3 (1.0)	0	0.484
NYHA II	170 (11.4)	0 (0.0%)	35 (9.9)	85 (11.7)	40 (12.7)	10 (14.7)	0.223
NYHA III	539 (36.1)	11 (39.3)	117 (33.1)	290 (39.8)	107 (34.0)	14 (20.6)	0.009
NYHA IV	279 (18.7)	4 (14.3)	47 (13.3)	114 (15.7)	80 (25.4)	34 (50.0)	< 0.001
Type of heart failure							0.002
HFrEF	665 (44.6)	15 (53.6)	184 (52.1)	321 (44.1)	121 (38.4)	24 (35.3)	0.003
HFmrEF	539 (36.1)	8 (28.6)	123 (34.8)	263 (36.1)	122 (38.7)	23 (33.8)	0.731
HFpEF	288 (19.3)	5 (17.9)	46 (13.0)	144 (19.8)	72 (22.9)	21 (30.9)	0.002
Medication							
ACEIs	524 (35.1)	6 (21.4)	138 (39.1)	269 (37.0)	98 (31.1)	13 (19.1)	0.003
ARBs	320 (21.4)	5 (17.9)	41 (11.6)	142 (19.5)	105 (33.3)	27 (39.7)	< 0.001
β blockers	968 (64.9)	18 (64.3)	249 (70.5)	485 (66.6)	183 (58.1)	33 (48.5)	< 0.001
CCBs	327 (21.9)	6 (21.4)	37 (10.5)	123 (16.9)	118 (37.5)	43 (63.2)	< 0.001
MRA	769 (51.5)	19 (67.9)	202 (57.2)	375 (51.5)	144 (45.7)	29 (42.6)	0.007
Diuretic	969 (64.9)	19 (67.9)	228 (64.6)	483 (66.3)	198 (62.9)	41 (60.3)	0.736
Digitalis	421 (28.2)	8 (28.6)	103 (29.2)	206 (28.3)	89 (28.3)	15 (22.1)	0.837
Nitrate esters	934 (62.6)	15 (53.6)	207 (58.6)	458 (62.9)	208 (66.0)	46 (67.6)	0.223

mmHg), the risk of heart failure rehospitalization was significantly increased in the SBP>150 mmHg group (*OR* 2.67, *95%CI* 1.15–6.18, *P* = 0.022). Compared with the reference group (110 < SBP≤130 mmHg), the 130 < SBP≤150 mmHg group had a lower risk of cardiac death (*OR* 0.43, *95%CI* 0.19–0.96, *P* = 0.039). (Table 4, Fig. 1a).

According to DBP, compared with the reference group (65 < DBP≤75 mmHg), the risk of cardiac death (*OR* 2.64, *95% CI* 1.15–6.05, *P* = 0.022) and all-cause death (*OR* 2.67, *95% CI* 1.20–5.93, *P* = 0.016) in the DBP≤55 mmHg group increased significantly; There was no significant difference in the risk of end points in other DBP groups (all *P* > 0.05). (Table 4, Fig. 1b).

3.4. Subgroup analysis

Subgroup analysis was performed according to different LVEF (LVEF <40% and LVEF ≥40%), and there was no significant difference between subgroups. The interaction *P* values of heart failure rehospitalization, cardiac death, all-cause death and composite endpoint in SBP group were 0.524, 0.818, 0.890 and 0.727, respectively. In DBP group, the values were 0.431, 0.802, 0.884 and 0.660, respectively. (all *P* > 0.05).

4. Discussion

In this retrospective cohort study of patients with HF, we examined the association between different BP levels and clinical endpoints 3 months after discharge, so as to explore the impact of the BP level on the short-term prognosis of patients with HF. The results showed that for patients hospitalized with HF, there were significant differences in the short-term prognosis after discharge because of different levels of BP at discharge (systolic or diastolic). There was an inverse J-curve between BP and prognosis in patients with HF. Low BP (SBP≤90 mmHg, DBP≤55 mmhg) was associated with the worst prognosis. In addition to the significantly increased risk of heart failure rehospitalization due to high SBP (SBP >150 mmHg), it seems that higher BP has a better prognosis, and the risk of events is lower when SBP is between 90 mmHg and 150 mmHg and DBP is more than 55 mmHg. And this phenomenon has no difference between different LVEF.

Many clinical evidences (the results of large clinical trials such as VALUE, INVEST, TNT, ONTARGET, PROVE IT-TIMI 22) tend to support the J-curve or U-curve relationship between BP and cardiovascular events and death risk [13], that is, when the BP level is too high or too low, it will increase the risk of adverse events, and the risk of adverse events of too high BP is more prominent than that of too low BP. The patient population of these studies included the general population with

Table 2
Baseline characteristics of HF patients divided by different diastolic blood pressure levels.

	Total n = 1492	DBP≤55 mmHg n = 65	55 < DBP≤65 mmHg n = 356	65 < DBP≤75 mmHg n = 575	75 < DBP≤85 mmHg n = 408	DBP > 85 mmHg n = 88	*P*
Male	937 (62.8)	34 (52.3)	210 (59.0)	357 (62.1)	267 (65.4)	69 (78.4)	0.003
Age	68.00 ± 12.48	70.85 ± 14.45	69.55 ± 11.35	68.53 ± 12.31	66.97 ± 12.45	60.91 ± 13.78	< 0.001
BNP,pg/ml	792.00 (531.75–1422.50)	694.00 (519.00–3333.00)	672.50 (502.50–1147.50)	814.00 (534.25–1587.75)	772.00 (543.50–1425.00)	1075.00 (528.50–1480.00)	0.610
NT proBNP,pg/ml	2854.00 (1491.50–6889.50)	4293.00 (1811.00–13281.50)	2985.50 (1508.50–6868.25)	2654.00 (1264.00–6345.00)	2808.50 (1552.75–6957.00)	3499.00 (2196.00–7483.00)	0.123
LVEF,%	40.00 (34.00–47.00)	41.00 (33.50–49.50)	40.00 (35.00–46.75)	40.00 (34.00–45.00)	40.50 (34.00–48.00)	42.00 (34.25–48.00)	0.349
Causes and comorbidities							
Coronary heart disease	1199 (80.4)	50 (76.9)	289 (81.2)	477 (83.0)	323 (79.2)	60 (68.2)	0.019
Hypertension	878 (58.8)	28 (43.1)	197 (55.3)	323 (56.2)	265 (65.0)	65 (73.9)	< 0.001
Diabetes	474 (31.8)	11 (16.9)	98 (27.5)	202 (35.1)	133 (32.6)	30 (34.1)	0.012
Cerebrovascular disease	351 (23.5)	14 (21.5)	92 (25.8)	131 (22.8)	96 (23.5)	18 (20.5)	0.765
Atrial fibrillation	399 (26.7)	14 (21.5)	87 (24.4)	157 (27.3)	119 (29.2)	22 (25.0)	0.506
CKD	274 (18.4)	17 (26.2)	56 (15.7)	93 (16.2)	78 (19.1)	30 (34.1)	< 0.001
Cardiac functional grading							0.022
NYHA I	12 (0.8)	0	8 (2.2)	0	2 (0.5)	2 (2.3)	0.002
NYHA II	170 (11.4)	8 (12.3)	33 (9.3)	67 (11.7)	52 (12.7)	10 (11.4)	0.659
NYHA III	539 (36.1)	25 (38.5)	112 (31.5)	214 (37.2)	159 (39.0)	29 (33.0)	0.229
NYHA IV	279 (18.7)	13 (20.0)	56 (15.7)	110 (19.1)	76 (18.6)	24 (27.3)	0.167
Type of heart failure							0.788
HFrEF	665 (44.6)	28 (43.1)	162 (45.5)	266 (46.3)	172 (42.2)	37 (42.0)	
HFmrEF	539 (36.1)	21 (32.3)	122 (34.3)	210 (36.5)	153 (37.5)	33 (37.5)	
HFpEF	288 (19.3)	16 (24.6)	72 (20.2)	99 (17.2)	83 (20.3)	18 (20.5)	
Medication							
ACEIs	524 (35.1)	17 (26.2)	141 (39.6)	203 (35.3)	137 (33.6)	26 (29.5)	0.132
ARBs	320 (21.4)	10 (15.4)	56 (15.7)	129 (22.4)	104 (25.5)	21 (23.9)	0.012
β blockers	968 (64.9)	35 (53.8)	220 (61.8)	385 (67.0)	270 (66.2)	58 (65.9)	0.172
CCBs	327 (21.9)	11 (16.9)	58 (16.3)	128 (22.3)	97 (23.8)	33 (37.5)	< 0.001
MRA	769 (51.5)	41 (63.1)	186 (52.2)	290 (50.4)	215 (52.7)	37 (42.0)	0.125
Diuretic	969 (64.9)	42 (64.6)	225 (63.2)	390 (67.8)	259 (63.5)	53 (60.2)	0.431
Digitalis	421 (28.2)	24 (36.9)	84 (23.6)	161 (28.0)	122 (29.9)	30 (34.1)	0.082
Nitrate esters	934 (62.6)	36 (55.4)	206 (57.9)	361 (62.8)	275 (67.4)	56 (63.6)	0.063

Table 1 , Table 2 : SBP: systolic blood pressure; DBP : diastolic blood pressure; BNP: brain natriuretic peptide; NT-proBNP : N-terminal pro-brain natriuretic peptide; LVEF : Left ventricular ejection fraction; CKD: chronic kidney dysfunction; NYHA : New York Heart Association classification of cardiac function; HFrEF : Heart failure with reduced ejection fraction; HFmrEF : Heart failure with mild reduced ejection fraction; HFpEF:Heart failure with preserved ejection fraction; ACEIs : Angiotensin converting enzyme inhibitors; ARBs : Angiotensin receptor blockers; CCB:Calcium channel blockers; MRA:Mineralocorticoid receptor antagonist.

Table 3
Comparison of endpoint events and event rates for different blood pressure groups.

BP(mmHg)	n	heart failure rehospitalization n (%)	P	cardiac death n (%)	P	all-cause death n (%)	P	composite end point n (%)	P
SBP at discharge									
SBP≤90	28	6 (21.43)	P < 0.001	6 (21.43)	P < 0.001	6 (21.43)	P = 0.017	6 (21.43)	P < 0.001
90 < SBP≤110	353	16 (4.53)		19 (5.38)		21 (5.95)		36 (10.20)	
110 < SBP≤130	728	27 (3.71)		40 (5.49)		45 (6.18)		72 (9.89)	
130 < SBP≤150	315	22 (6.98)		8 (2.54)		17 (5.40)		39 (12.38)	
SBP > 150	68	13 (19.12)		3 (4.41)		6 (8.82)		19 (27.94)	
DBP at discharge									
DBP≤55	65	6 (9.23)	P = 0.236	9 (13.85)	P = 0.015	10 (15.38)	P = 0.007	13 (20.00)	P = 0.203
55 < DBP≤65	356	15 (4.21)		21 (5.90)		30 (8.43)		42 (11.80)	
65 < DBP≤75	575	35 (6.09)		26 (4.52)		29 (5.04)		64 (11.13)	
75 < DBP≤85	408	20 (4.90)		17 (4.17)		22 (5.39)		41 (10.05)	
DBP > 85	88	8 (9.09)		3 (3.41)		4 (4.55)		12 (13.64)	

hypertension, as well as those with hypertension complicated coronary heart disease, diabetes, chronic kidney disease, stroke/TIA, and the elderly [13]. Nevertheless, the J-curve of BP is still controversial [14, 15].

Unlike people with hypertension, the relationship between BP and the risk of adverse events seems to be more controversial and uncertain for people with HF. Although studies have reported that there is a U-shaped curve or linear relationship between SBP and the risk of all-cause death in HF patients.[3]However, there is more evidence that in patients with HF, higher BP is associated with a better prognosis, while lower BP is associated with poor survival. A meta-analysis assessed the association between SBP and mortality in patients with chronic heart failure (CHF).

Table 4
Effects of different BP levels on outcomes of HF patients (adjusted).

	heart failure rehospitalization		cardiac death		all-cause death		composite end point	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
SBP at discharge (mmHg)								
SBP≤90 rowhead	8.16 (2.88,23.11)	< 0.001	5.43 (1.97,14.96)	0.001	4.85 (1.76,13.36)	0.002	2.76 (1.03,7.41)	0.044
90 < SBP ≤110 rowhead	1.49 (0.77,2.87)	0.238	1.06 (0.59,1.91)	0.841	1.12 (0.64,1.95)	0.701	1.24 (0.79,1.93)	0.356
110 < SBP ≤130 rowhead	1.00 (ref.)	–	1.00 (ref.)	–	1.00 (ref.)	–	1.00ref.)	–
130 < SBP ≤150 rowhead	1.49 (0.80,2.80)	0.212	0.43 (0.19,0.96)	0.039	0.76 (0.41,1.41)	0.382	1.05 (0.66,1.66)	0.849
SBP > 150 rowhead	2.67 (1.15,6.18)	0.022	0.58 (0.16,2.13)	0.413	0.87 (0.32,2.34)	0.779	1.72 (0.87,3.40)	0.119
DBP at discharge (mmHg)								
DBP≤55 rowhead	1.23 (0.48,3.16)	0.664	2.64 (1.15,6.05)	0.022	2.67 (1.20,5.93)	0.016	1.54 (0.77,3.10)	0.222
55 < DBP≤65 rowhead	0.67 (0.36,1.26)	0.209	1.24 (0.68,2.26)	0.484	1.69 (0.99,2.91)	0.056	1.05 (0.68,1.60)	0.839
65 < DBP≤75 rowhead	1.00 (ref.)	–	1.00 (ref.)	–	1.00 (ref.)	–	1.00 (ref.)	–
75 < DBP≤85 rowhead	0.78 (0.44,1.39)	0.398	1.02 (0.54,1.93)	0.946	1.20 (0.67,2.15)	0.54	0.94 (0.61,1.44)	0.765
DBP > 85 rowhead	1.27 (0.54,3.02)	0.583	1.04 (0.30,3.59)	0.955	1.17 (0.39,3.52)	0.78	1.33 (0.66,2.70)	0.422

Table 3 Table 4 : BP: blood pressure; SBP : systolic blood pressure; DBP : diastolic blood pressure.

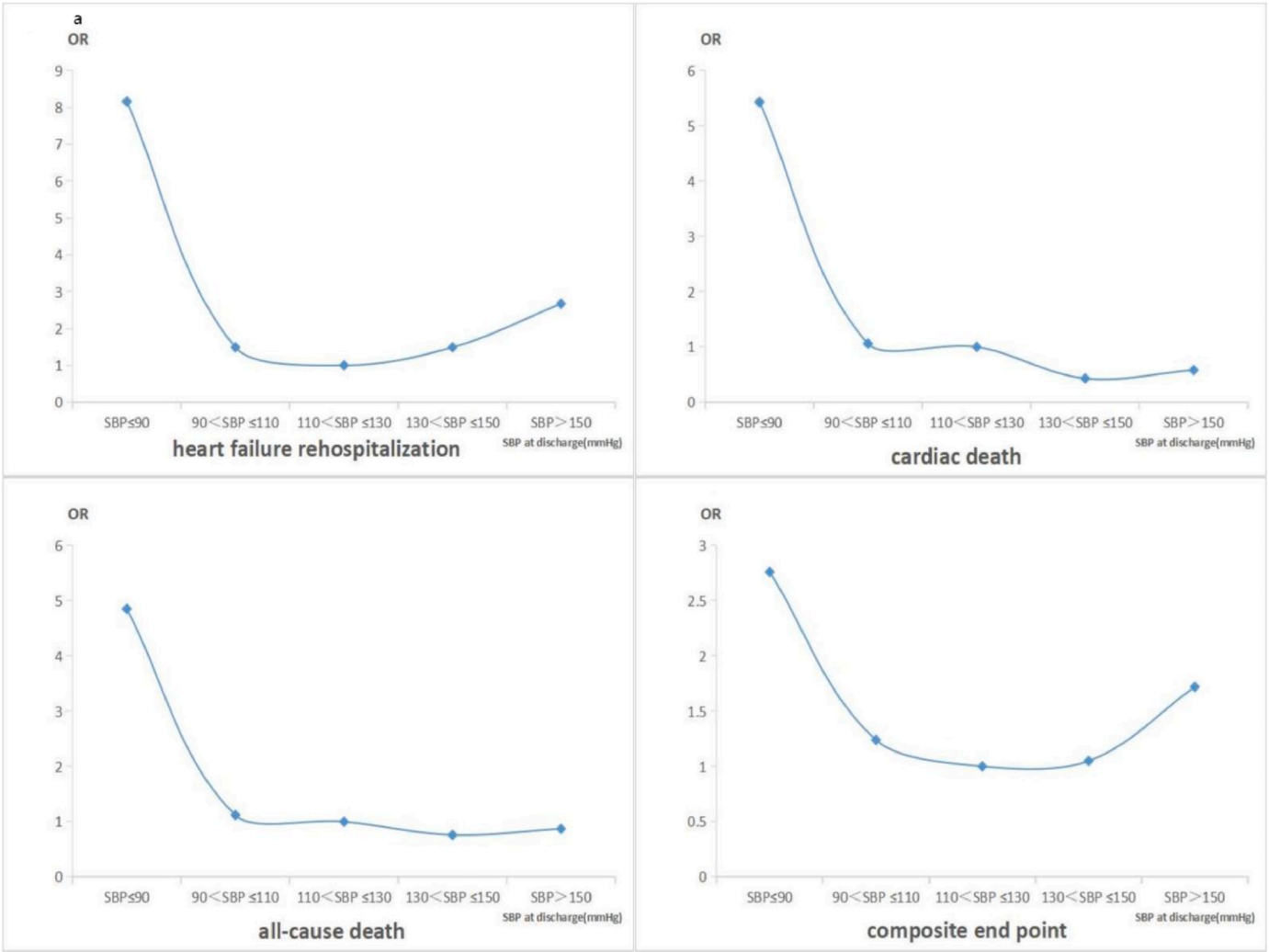

Fig. 1a. odds ratios (adjusted) in HF patients with different SBP levels.

[9]An analysis included 10 studies involving 8088 patients with CHF, the results showed that patients with higher SBP had a better prognosis, and the risk of death decreased by 13% for every 10 mmHg increase in SBP in patients with CHF·In addition, there was a quantitative relationship between SBP and mortality, and the lower the basal BP, the greater the impact on death.[9]In a post-hoc analysis of a large cohort of patients with acute heart failure (AHF), using SBP as a continuous variable, each 10 mmHg increase in SBP was associated with a 7% decrease in the risk of 180-day all-cause death and a 10% decrease in the risk of a 15-day short-term composite event. Even in the absence of hypotension, patients with SBP in the normal range (SBP 125–135 mmHg) have a worse prognosis than patients with mild to moderately elevated SBP (SBP136-180 mmHg).[16]To assess the association between DBP and cardiovascular events and death in HFpEF patients, a post-hoc analysis of TOPCAT data showed that patients with DBP of 60–69 mmHg had a significantly increased risk of events compared with patients with DBP

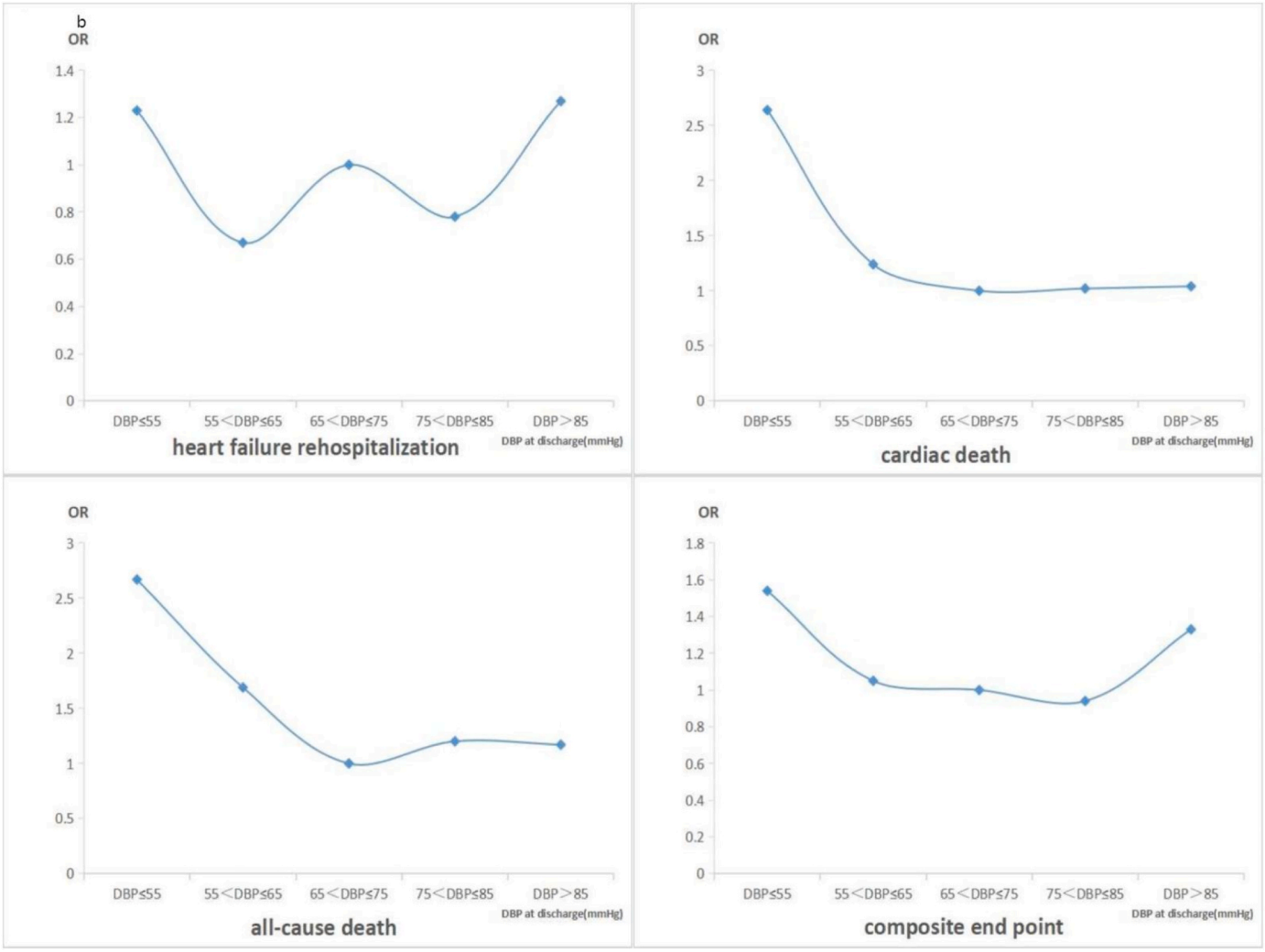

Fig. 1b. odds ratios (adjusted) in HF patients with different DBP levels.

of 80–89 mmHg (*HR* 1.52, *95%CI* 1.23–1.87), and patients with DBP<60 mmHg had a higher risk of events (*HR* 2.19, *95%CI* 1.72–2.78), suggesting that low DBP increased the risk of adverse outcomes in patients with HFpEF.[8]Although the populations of the above studies are different, consistent with our results, they all support that higher BP in patients with HF has a better prognosis.

A prospective, multicenter study on AHF in South Korea (KorAHF) observed the relationship between BP and clinical outcomes of patients with HF. 5625 hospitalized patients with AHF were followed up for an average of 2.2 years. The results showed that there was a reverse J-curve relationship between BP and the risk of all-cause death in patients with HF. The lowest risk value (point J) SBP/DBP was 132.4/74.2 mmHg respectively, of which the lowest risk value of HFrEF was 136.0/76.6 mmHg, HFpEF is 127.9/72.7 mmHg.Although there is an increased risk of death from low or high BP, the risk of death from low BP is greater [10]. Compared with this study in Korea, although our study has a short follow-up time and focuses on the short-term prognosis of hospitalized patients with HF after discharge (followed up for 3 months after discharge), we also observed a reverse J-curve relationship between BP and clinical endpoint events in patients with HF.

The possible mechanism of worse prognosis in HF patients with hypotension in this study is speculated to be related to the following factors. Firstly, the formation of arterial blood pressure depends on cardiac pump function and peripheral vascular resistance. Low cardiac output caused by pump failure is related to hypotension. Patients with HF will gradually decline their systolic function as their condition progresses, so lower BP partly reflects worse heart function. Even for patients with a past history of hypertension, in the late stage of HF, BP tends to be normal or lower than normal, which is called “decapitated hypertension” phenomenon [17]. On the contrary, higher BP often reflects that patients with HF still have better myocardial reserve and relatively good cardiac pump function. Second, low DBP causes coronary hypoperfusion, resulting in an increased risk of cardiac ischemic events. Third, HF patients with hypotension often cannot tolerate the drug treatment recommended by the guidelines, such as ACEIs or ARBs, angiotensin receptor neprilysin inhibition (ARNI), diuretics and β blockers, and these drugs are just the main treatment means to improve the symptoms and prognosis of patients with HF, which makes the treatment of these patients more difficult and complex, and the prognosis worse.

4.1. Limitations

This study is a retrospective cohort study, and there are inevitably some confounding factors. First of all, the research population of this study is concentrated in one city in China, and there is some selection bias. Secondly, after stratification of the population with BP, the number of cases in the low and high BP groups is relatively small, and the number of cases in each group is unbalanced, which may bias the results. Thirdly, this study did not fully analyze the effects of drug treatment

(drug species and dose) on BP and prognosis between different groups. In addition, in this study, the BP of patients is the BP at discharge. There was no BP monitoring and follow-up within 3 months after discharge, so there was a lack of dynamic BP data. The relationship between the dynamic evolution of BP and the prognosis of patients with BP, especially the impact on the long-term prognosis, needs to be further observed. Finally, this study covers hospitalized patients from 2014 to 2016, which is relatively early and should be verified using data collected in recent years.

5. Conclusion

Our findings support the inverse J-curve relationship between BP and short-term prognosis in patients with HF. Low BP is associated with the worst prognosis, while higher BP tends to have a better prognosis. Therefore, it is recommended that the BP of HF patients should not be controlled too low compared with patients without HF. In the future, more targeted, well-designed and large-scale randomized controlled trials are needed to evaluate the optimal blood pressure target of HF patients.

Author contributions

N.-X.J. and L.-Z.M. drafted the manuscript together. L.-Z.M. and T.-J. L. designed the study. L.-Z.M., K.-Y., Mingxue.-L. and Rongrong Zhong completed information collection and follow up. N.-X.J. analyzed the data, prepared the Tables and Figures.All authors have read and agreed to the published version of the manuscript.

Statement of ethics

Approved by the Medical Ethics Committee of Tianjin Medical University General Hospital (Approval No.: IRB2017-029-01). All patients were informed of the nature and aims of surveys and signed a written informed consent.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcrp.2023.200169.

References

[1] Simon Stewart, Ekman Inger, Ekman Tor, Odén Anders, Rosengren Annika, Population impact of heart failure and the most common forms of cancer: a study of 1 162 309 hospital cases in Sweden (1988 to 2004), Circ Cardiovasc Qual Outcomes 3 (6) (2010) 573–580.

[2] Heart failure group of Chinese society of cardiology of Chinese medical association, Chinese heart failure association of Chinese medical doctor association, editorial board of Chinese journal of cardiology, Chinese guidelines for the diagnosis and treatment of heart failure 2018. Chin J Cardiol 46 (10) (2018) 760–789.

[3] S. Ather, W. Chan, A. Chillar, D. Aguilar, A.M. Pritchett, K. Ramasubbu, X. H. Wehrens, A. Deswal, B. Bozkurt, Association of systolic blood pressure with mortality in patients with heart failure with reduced ejection fraction: a complex relationship, Am. Heart J. 161 (3) (2011) 567–573.

[4] M. Gheorghiade, W.T. Abraham, N.M. Albert, B.H. Greenberg, C.M. O'Connor, L. She, W.G. Stough, C.W. Yancy, J.B. Young, G.C. Fonarow, Systolic blood pressure at admission, clinical characteristics, and outcomes in patients hospitalized with acute heart failure, JAMA 296 (18) (2006) 2217–2226. OPTIMIZE-HF Investigators and Coordinators.

[5] W.T. Abraham, G.C. Fonarow, N.M. Albert, W.G. Stough, M. Gheorghiade, B. H. Greenberg, C.M. O'Connor, J.L. Sun, C.W. Yancy, J.B. Young, Predictors of in-hospital mortality in patients hospitalized for heart failure: insights from the organized program to initiate lifesaving treatment in hospitalized patients with heart failure (OPTIMIZE-HF), J. Am. Coll. Cardiol. 52 (5) (2008) 347–356. OPTIMIZE-HF Investigators and Coordinators.

[6] C. Arundel, P.H. Lam, G.S. Gill, S. Patel, G. Panjrath, C. Faselis, M. White, C. J. Morgan, R.M. Allman, W.S. Aronow, S.N. Singh, G.C. Fonarow, A. Ahmed, Systolic blood pressure and outcomes in patients with heart failure with reduced ejection fraction, J. Am. Coll. Cardiol. 73 (24) (2019) 3054–3063.

[7] A. Tsimploulis, P.H. Lam, C. Arundel, S.N. Singh, C.J. Morgan, C. Faselis, P. Deedwania, J. Butler, W.S. Aronow, C.W. Yancy, G.C. Fonarow, A. Ahmed, Systolic blood pressure and outcomes in patients with heart failure with preserved ejection fraction, JAMA Cardiology 3 (4) (2018) 288–297.

[8] T. Tsujimoto, H. Kajio, Low diastolic blood pressure and adverse outcomes in heart failure with preserved ejection fraction, Int. J. Cardiol. 263 (2018) 69–74.

[9] C.E. Raphael, Z.I. Whinnett, J.E. Davies, M. Fontana, E.A. Ferenczi, C.H. Manisty, J. Mayet, D.P. Francis, Quantifying the paradoxical effect of higher systolic blood pressure on mortality in chronic heart failure, Heart (British Cardiac Society) 95 (1) (2009) 56–62.

[10] S.E. Lee, H.Y. Lee, H.J. Cho, W.S. Choe, H. Kim, J.O. Choi, E.S. Jeon, M.S. Kim, K. K. Hwang, S.C. Chae, S.H. Baek, S.M. Kang, D.J. Choi, B.S. Yoo, K.H. Kim, M. C. Cho, J.J. Kim, B.H. Oh, Reverse J-curve relationship between on-treatment blood pressure and mortality in patients with heart failure, JACC. Heart Failure 5 (11) (2017) 810–819.

[11] G.C. Oh, H.J. Cho, Blood pressure and heart failure, Clinical Hypertension 26 (2020) 1.

[12] P. Ponikowski, A.A. Voors, S.D. Anker, H. Bueno, J.G. Cleland, A.J. Coats, V. Falk, J.R. González-Juanatey, V.P. Harjola, E.A. Jankowska, M. Jessup, C. Linde, P. Nihoyannopoulos, J.T. Parissis, B. Pieske, J.P. Riley, G.M. Rosano, L.M. Ruilope, F. Ruschitzka, F.H. Rutten, P. van der Meer, , Authors/Task Force Members, Document Reviewers, 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC, Eur. J. Heart Fail. 18 (8) (2016) 891–975.

[13] M. Banach, W.S. Aronow, Blood pressure j-curve: current concepts, Curr. Hypertens. Rep. 14 (6) (2012) 556–566.

[14] L. Hansson, Antihypertensive treatment: does the J-curve exist? Cardiovasc. Drugs Ther. 14 (4) (2000) 367–372.

[15] M. Böhm, S. Ewen, Blood pressure risk associations in heart failure: true effects or inverse causality? JACC. Heart failure 5 (11) (2017) 820–822.

[16] J. Grand, K. Miger, A. Sajadieh, L. Køber, C. Torp-Pedersen, G. Ertl, J. López-Sendón, A. Pietro Maggioni, J.R. Teerlink, N. Sato, C. Gimpelewicz, M. Metra, T. Holbro, O.W. Nielsen, Systolic blood pressure and outcome in patients admitted with acute heart failure: an analysis of individual patient data from 4 randomized clinical trials, J. Am. Heart Assoc. 10 (18) (2021), e022288.

[17] F.H. Messerli, S.F. Rimoldi, S. Bangalore, The transition from hypertension to heart failure: contemporary update, JACC Heart Fail 5 (8) (2017) 543–551.