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RESEARCH PAPER

Control of blood pressure in older patients with heart failure and the risk of mortality: a population-based prospective cohort study

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Abstract

Background: treatment goals for blood pressure (BP) lowering in older patients with heart failure (HF) are unclear.
Objective: to assess whether BP control < 140/90 mmHg is associated with a decreased risk of mortality in older HF patients.

Design: population-based prospective cohort study.

Setting/subjects: participants of the Berlin Initiative Study, a prospective cohort of community-dwelling older adults launched in 2009. Clinical information was obtained in face-to-face interviews and linked to administrative healthcare data.

Methods: Cox proportional hazards models estimated adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) of cardiovascular death and all-cause mortality associated with normalised BP (systolic BP < 140 mmHg and diastolic BP < 90 mmHg) compared with non-normalised BP (systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg) in HF patients. The primary analysis considered only baseline BP ('time-fixed'); an additional analysis updated BP during follow-up ('time-dependent').

Results: at baseline, 544 patients were diagnosed with HF and treated with antihypertensive drugs (mean age 82.8 years; 45.4% female). During a median follow-up of 7.5 years and compared with non-normalised BP, normalised BP was associated with similar risks of cardiovascular death (HR, 1.24; 95% CI, 0.84–1.85) and all-cause mortality (HR, 1.16; 95% CI, 0.89–1.51) in the time-fixed analysis but with increased risks of cardiovascular death (HR, 1.79; 95% CI, 1.23–2.61) and all-cause mortality (HR, 1.48; 95% CI, 1.15–1.90) in the time-dependent analysis.

Conclusions: BP control < 140/90 mmHg was not associated with a decreased risk of mortality in older HF patients. The increased risk in the time-dependent analysis requires further corroboration.

Keywords: epidemiology, cardiovascular death, antihypertensive treatment, geriatric cohort, older people

Key Points

- Our observational study included 544 older patients (mean age 83 years) with heart failure treated with antihypertensive drugs.
- During a median follow-up of 7.5 years and compared with non-normalised blood pressure (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg), normalised blood pressure (systolic blood pressure < 140 mmHg and diastolic blood pressure < 90 mmHg) was associated with similar risks of cardiovascular death and all-cause mortality in a time-fixed analysis.
- In a time-dependent analysis, normalised blood pressure was associated with a 79% increase in the relative risk of cardiovascular death and a 48% increase in the relative risk of all-cause mortality.

Introduction

Heart failure (HF) affects approximately 26 million people worldwide [1], with a prevalence of up to 30% in individuals over 85 years [2–4]. HF is the leading cause of hospitalisation among older adults and is associated with high rates of morbidity and mortality and with an increased risk of developing new disability [5–7]. Accordingly, the importance of treating HF in older populations is highlighted in current guidelines [8,9].

Hypertension is an important risk factor of HF being responsible for every tenth new case [10]. Moreover, in patients with HF, elevated blood pressure (BP) levels have been linked to worse clinical outcomes [11]. Thus, BP control is advocated as part of the holistic approach of HF management [8,12]. However, exact treatment goals for BP lowering in HF patients are often unclear, and specific recommendations are based on expert consensus and extrapolation from populations without HF [8,12,13].

This knowledge gap is even more pronounced when it comes to older adults. The two largest randomised controlled trials (RCTs) to date assessing the effects of BP lowering in older patients, the Hypertension in the Very Elderly Trial (HYVET) [14] and the subgroup analysis of the Systolic Blood Pressure Intervention Trial (SPRINT) [15], systematically excluded individuals with HF. Observational studies in the area had limited follow-up, were restricted to hospitalised patients, were not based on contemporary data, and applied retrospective designs [16–18]. Thus, given the scarcity and limitations of available evidence, our population-based prospective cohort study assessed whether BP control is associated with a decreased risk of cardiovascular death and all-cause mortality in community-dwelling older adults with HF.

Methods

Data source

We used data from the Berlin Initiative Study (BIS), an ongoing, population-based, prospective cohort study initiated in 2009 in Berlin, Germany, to evaluate kidney function in older adults [19]. Inclusion criteria of the BIS were membership in the 'AOK Nordost - Die Gesundheitskasse' statutory health insurance, residency in Berlin and age ≥70 years. Exclusion criteria were dialysis treatment or kidney transplantation. The BIS population (described in detail elsewhere [20]) is comparable to the older German general population with regard to common morbidities [21–24]. Recruitment of participants was conducted from November 2009 to June 2011 at 13 study sites (physician practices) in Berlin using a random sample of insurants. At the initial study visit, participants were interviewed face-to-face based on a structured questionnaire to assess demographics, lifestyle variables (e.g. smoking, alcohol consumption, physical exercise), medications and comorbidities. Anthropometric variables (e.g. body mass index [BMI], BP [defined below]) were measured and blood and urine samples were collected. These procedures were repeated at biennial follow-up visits. Given Germany's universal healthcare system with free access to healthcare services and the independence between the BIS staff measuring BP and the staff of the practice, we do not expect that the inclusion of individuals in our study affected their medical treatment. To enhance comorbidity assessment, participants' data were linked to the administrative databases of the health insurance which included inpatient and outpatient diagnoses (coded using the International Statistical Classification of Diseases, 10th revision [ICD-10]). All participants gave written informed consent. The study was approved by the local ethics committee.

Study population

Out of the BIS population, we assembled a study cohort comprising all participants who met both of the following inclusion criteria at the initial study visit: treatment with ≥1 antihypertensive medication (except for loop diuretic monotherapy) and diagnosis of HF. HF was defined as ≥1 inpatient or ≥2 outpatient diagnostic codes (in two different quarters) in the 3 years before the initial study visit (ICD-10 codes: I11.0, I13.0, I13.2, I50.x). Cohort entry was the date of the initial study visit. All patients were followed from cohort entry until the occurrence of one of the outcomes (defined below) or the end of study period (December 2018).

Exposure definition

We classified patients into one of the following two categories according to their BP status at cohort entry: 'normalised BP', defined as systolic BP (SBP) < 140 mmHg and diastolic BP (DBP) < 90 mmHg and 'non-normalised BP', defined as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg. Based on recommendations by the European Society of Cardiology and the European Society of Hypertension, we calculated BP as the mean of two office measurements within ten minutes; patients were seated before measurement for 5 min with legs uncrossed and not talking [13]. Using a *time-fixed* exposure definition analogous to the *intention-to-treat* approach in RCTs, patients were assumed to retain their BP status for the whole duration of follow-up.

Covariates

We considered the following covariates at cohort entry: age (modelled flexibly using restricted cubic splines to account for potential non-linear associations with the outcomes), sex, BMI, smoking (ever, never), alcohol consumption (less than once monthly, once monthly to twice weekly, or more than twice weekly) and physical exercise (>30 min; less than once weekly, one to five times weekly, or more than five times weekly). Moreover, we assessed estimated glomerular filtration rate (<60 mL/min per 1.73 m^2, ≥60 mL/min per 1.73 m^2; calculated using the BIS2 equation [25]) and albuminuria (albumin-to-creatinine ratio ≥ 30 mg/g in spot urine analysis) as markers of kidney function. We also assessed several comorbidities at cohort entry: atrial fibrillation, diabetes, hyperlipidemia, myocardial infarction (MI), stroke, chronic obstructive pulmonary disease and cancer. The covariates were defined using ICD-10 codes, laboratory values and patient reported information (Table S1). Finally, we considered duration of treated hypertension and overall number of antihypertensive medications at cohort entry as proxies of disease severity.

Outcome definition

The study outcomes were cardiovascular death and all-cause mortality. We ascertained date of death from the administrative databases of the health insurance (available in all cases) and cause of death from death certificates and hospital discharge notes for in-hospital deaths (available in 90% of cases). Cause of death was assessed independently by three physicians (NE, ES, MvdG); disagreements were resolved through discussion.

Statistical analyses

Cox proportional hazards models yielded hazard ratios (HRs) with 95% confidence intervals (CIs) of the outcomes associated with normalised BP compared with non-normalised BP, adjusting for all covariates mentioned above. To assess a possible effect modification by HF, we repeated the analyses among patients receiving antihypertensive medications at cohort entry but *without* HF.

Additional analyses

We conducted an analysis using a *time-dependent* exposure definition to account for potential exposure misclassification during follow-up, updating the BP status of each patient at every biennial study visit. Thus, each patient was allowed to contribute person-time to different exposure categories during follow-up. Moreover, we updated all covariates at every study visit except for sex (no anticipated changes during follow-up) and duration of treated hypertension (not captured at follow-up visits) to account for potential time-dependent confounding. As in the primary analysis, we also conducted the time-dependent analysis in non-HF patients.

In secondary analyses among patients with HF, we assessed possible effect modifications by age (70–79 versus ≥80 years) and prior cardiovascular events (i.e. stroke and/or MI). In sensitivity analyses among patients with HF, we used a stricter HF definition additionally requiring use of HF specific medications (i.e. angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers or beta-blockers) at cohort entry and imposed a 1-year lag period to assess the potential impact of reverse causality, given the terminal decline in BP at the end-of-life. In the latter analysis, events occurring during the first year of follow-up (i.e. during the lag period) were not counted. Finally, in a post-hoc sensitivity analysis we additionally adjusted for use of different antihypertensive drug classes.

We also assessed the association between SBP as continuous variable and the risk of cardiovascular death and all-cause mortality, modelling SBP flexibly using natural splines with two interior knots to account for potential non-linear associations between SBP and the outcomes (reference: SBP 140 mmHg). A two-tailed P value < 0.05 was considered significant. All statistical analyses were conducted with SPSS (Version 25.0; IBM Corp, Armonk, NY) and R (Version 3.4.2; R Foundation for Statistical Computing, Vienna, Austria).

Results

Among 1,623 BIS participants treated with antihypertensive drugs at cohort entry, 544 (33.5%) had a diagnosis of HF (Figure 1). Of those, 255 (46.9%) showed normalised BP below 140/90 mmHg, while 289 (53.1%) had non-normalised BP. In the non-HF subcohort (n = 1,079), 380 (35.2%) patients showed normalised BP and 699 (64.8%) non-normalised BP. Table 1 shows the characteristics of patients with and without HF classified by BP control. As expected, patients with HF were older, more likely to be male and to have ever smoked, less likely to conduct physical exercise, and had a higher comorbidity burden, compared with patients without HF. Among HF patients, those with normalised BP were more likely to have ever smoked and had a higher prevalence of reduced kidney function, atrial fibrillation, prior cardiovascular events and chronic obstructive pulmonary disease, but a lower prevalence of

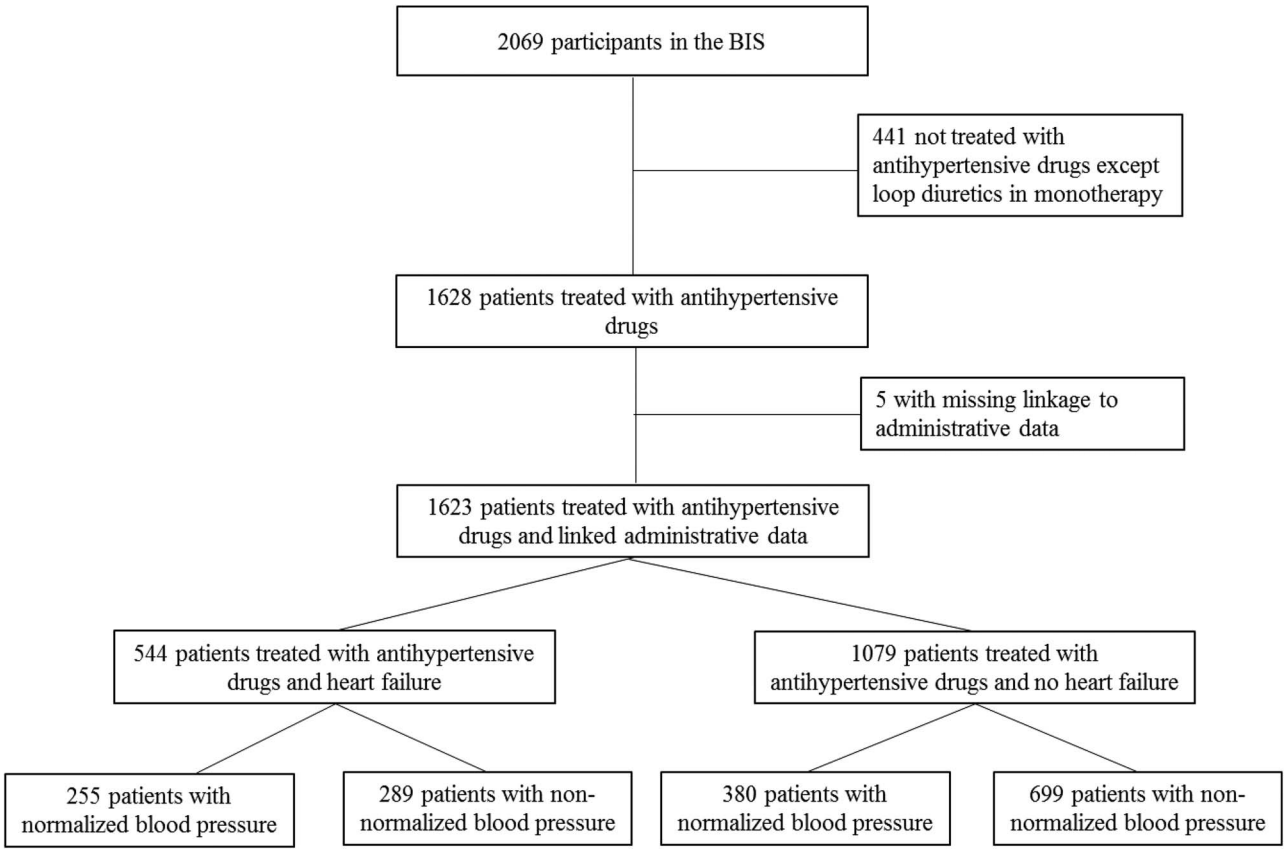

Figure 1. Flowchart with the construction of the study cohort. Abbreviation: BIS, Berlin Initiative Study.

albuminuria and diabetes than those with non-normalised values.

In HF patients, the median (interquartile range) follow-up for the outcome cardiovascular death was 7.5 (4.1–8.3) years, generating a total follow-up of 3,267 person-years (numbers for all-cause mortality almost identical). During the study period, 136 HF patients died of cardiovascular causes (crude incidence rate, 4.2 per 100 person-years) and 295 of any cause (crude incidence rate, 8.9 per 100 person-years). Compared with non-normalised BP, normalised BP in HF patients was associated with similar risks of cardiovascular death (HR, 1.24; 95% CI, 0.84–1.85) and all-cause mortality (HR, 1.16; 95% CI, 0.89–1.51) (Table 2). The effect estimates in non-HF patients were comparable to those in HF patients (Table 2).

The time-dependent analyses in HF patients yielded increased risks of cardiovascular death (HR, 1.79; 95% CI, 1.23–2.61) and all-cause mortality (HR, 1.48; 95% CI, 1.15–1.90) associated with normalised BP, compared with non-normalised BP (Table 3). Such statistically significant increased risks were not observed in non-HF patients (Table 3).

In secondary analyses among HF patients, age and prior cardiovascular events did not modify the associations (Figure 2; Tables S2 and S3). Sensitivity analyses among HF patients led to consistent results with the primary analysis (Tables S4 and S5). Finally, modelling SBP as a continuous variable showed an increased risk of cardiovascular death associated with values <120 mmHg, while a numerically increased risk of all-cause mortality associated with values <120 mmHg did not reach statistical significance. Inferences about the mortality risks with strongly increased SBP were challenging due to the low number of patients in this subgroup (Figures S1 and S2).

Discussion

Our population-based prospective cohort study showed that when compared with non-normalised BP, normalised BP is not associated with a decreased risk of mortality in older HF patients. Considering potential changes in BP control during follow-up corroborated the absence of clinical benefit associated with normalised BP in this vulnerable population and even suggested an increased risk of mortality. Repeating the analyses in older non-HF patients yielded no association between mortality risk and normalised BP.

BP control is currently recommended for all patients with HF [8,12]. According to the European guidelines, antihypertensive treatment in this population should be initiated when BP is >140/90 mmHg, while reductions <120/70 mmHg should be avoided [13]. However, specific recommendations for older HF patients are lacking. US guidelines recommend SBP < 130 mmHg in all HF patients

Table 1. Baseline characteristics of patients receiving antihypertensive medications with and without HF*

Characteristic	Heart failure		No heart failure	
	Normalised BP ($n = 255$)	Non-normalised BP ($n = 289$)	Normalised BP ($n = 380$)	Non-normalised BP ($n = 699$)
Age in years, mean (SD)	83.0 (6.6)	82.7 (6.9)	79.7 (6.1)	79.7 (6.4)
Female sex	111 (43.7)	136 (47.1)	214 (56.3)	387 (55.4)
Body mass index in kg/m^2, mean (SD)	28.5 (4.7)	28.5 (4.5)	27.8 (4.1)	27.9 (4.1)
≥30	87 (34.1)	97 (33.6)	109 (28.7)	181 (25.9)
<30	168 (65.9)	192 (66.4)	271 (71.3)	517 (74.0)
Unknown	0 (0)	0 (0)	0 (0)	1 (0.1)
Smoking status				
Ever	154 (60.4)	155 (53.6)	187 (49.2)	320 (45.8)
Never	101 (39.6)	134 (46.4)	192 (50.5)	378 (54.1)
Unknown	0 (0)	0 (0)	1 (0.3)	1 (0.1)
Alcohol consumption				
Less than once monthly	126 (49.4)	144 (49.8)	171 (45.0)	304 (43.5)
Once monthly to twice weekly	81 (31.8)	85 (29.4)	145 (38.2)	241 (34.5)
More than twice weekly	47 (18.4)	58 (20.1)	61 (16.0)	146 (20.9)
Unknown	1 (0.4)	2 (0.7)	3 (0.8)	8 (1.1)
Physical exercise				
Less than once weekly	89 (34.9)	100 (34.6)	81 (21.3)	173 (24.7)
One to five times weekly	114 (44.7)	124 (42.9)	190 (50.0)	339 (48.5)
More than five times weekly	52 (20.4)	65 (22.5)	106 (27.9)	187 (26.8)
Unknown	0 (0)	0 (0)	3 (0.8)	0 (0)
Markers of kidney function				
$eGFR_{BIS2}$ in ml/min per 1.73m^2, mean (SD)	49.4 (15.4)	52.4 (14.6)	58.2 (14.5)	59.1 (14.4)
≥60	68 (26.7)	94 (32.5)	172 (45.3)	334 (47.8)
<60	186 (72.9)	195 (67.5)	208 (54.7)	365 (52.2)
Unknown	1 (0.4)	0 (0)	0 (0)	0 (0)
Albuminuria	74 (29.1)	134 (46.7)	69 (18.4)	185 (26.7)
Comorbidities				
Atrial fibrillation	106 (41.6)	90 (31.1)	63 (16.6)	93 (13.3)
Diabetes mellitus	76 (29.9)	104 (36.0)	110 (28.9)	187 (26.8)
Hyperlipidemia	166 (65.4)	184 (63.7)	219 (57.6)	455 (65.1)
Prior myocardial infarction	83 (32.9)	70 (24.7)	60 (15.8)	77 (11.2)
Prior stroke	47 (18.7)	39 (13.8)	37 (9.8)	77 (11.2)
Chronic obstructive pulmonary disease	101 (39.6)	94 (32.5)	96 (25.3)	122 (17.5)
Cancer	60 (23.5)	69 (23.9)	82 (21.6)	154 (22.0)
Duration of treated hypertension in years, mean (SD)	15.1 (11.6)	15.8 (11.9)	14.2 (11.3)	13.8 (10.5)
Number of antihypertensive medications, mean (SD)	2.7 (1.1)	2.5 (1.1)	2.0 (1.0)	2.0 (1.0)
Angiotensin-converting enzyme inhibitors	145 (56.9)	143 (49.5)	175 (46.1)	349 (49.9)
Angiotensin II receptor blockers	78 (30.6)	92 (31.8)	118 (31.1)	206 (29.5)
Calcium channel blockers[c]	82 (32.2)	99 (34.3)	134 (35.3)	238 (34.0)
Beta-blockers	180 (70.6)	200 (69.2)	212 (55.8)	372 (53.2)
Diuretics	190 (74.5)	204 (70.6)	204 (53.7)	379 (54.2)

Abbreviations: BP, blood pressure; SD, standard deviation; eGFR, estimated glomerular filtration rate; BIS, Berlin Initiative Study. *Values are numbers (percentages) unless stated otherwise. [a]Systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg. [b]Systolic BP < 140 mmHg and diastolic BP < 90 mmHg. [c]Calcium channel blockers not recommended in HF (diltiazem, verapamil, nifedipine) were rarely used among patients with this condition (normalised BP group: 0.4% diltiazem, 2.0% verapamil, 1.6% nifedipine/non-normalised BP group: 1.4% diltiazem, 2.4% verapamil, 2.4% nifedipine).

Table 2. Crude and adjusted HRs of cardiovascular death and all-cause mortality associated with normalised blood pressure in older adults with or without HF

Groups	Number of patients	Number of events	Person-years	Incidence rate[c]	Crude HR (95% CI)	Adjusted HR[d] (95% CI)	*P* value for interaction
Cardiovascular death*							
Heart failure							
Non-normalised BP[a]	285	73	1,786	4.1	Reference	Reference	
Normalised BP[b]	251	63	1,481	4.3	1.05 (0.75–1.47)	1.24 (0.84–1.85)	
No heart failure							0.467
Non-normalised BP[a]	692	102	4,896	2.1	Reference	Reference	
Normalised BP[b]	375	43	2,601	1.7	0.80 (0.56–1.14)	0.97 (0.66–1.41)	
All-cause mortality							
Heart failure							
Non-normalised BP[a]	289	154	1,815	8.5	Reference	Reference	
Normalised BP[b]	255	141	1,504	9.4	1.12 (0.89–1.40)	1.16 (0.89–1.51)	
No heart failure							0.565
Non-normalised BP[a]	699	237	4,935	4.8	Reference	Reference	
Normalised BP[b]	380	123	2,635	4.7	0.97 (0.78–1.21)	1.08 (0.85–1.36)	

Abbreviations: BP, blood pressure; HR, hazard ratio; CI, confidence interval; SBP, systolic BP; DBP, diastolic BP. *Due to lack of data regarding cause of death, 1,603 of the overall 1,623 patients were included in the analyses on cardiovascular death. [a]SBP ≥ 140 mmHg or DBP ≥ 90 mmHg. [b]SBP < 140 mmHg and DBP < 90 mmHg. [c]Per 100 person-years. [d]Adjusted for age, sex, BMI, smoking status, alcohol consumption, physical exercise, estimated glomerular filtration rate, albuminuria, atrial fibrillation, diabetes mellitus, hyperlipidemia, prior myocardial infarction, prior stroke, chronic obstructive pulmonary disease, cancer, duration of treated hypertension and overall number of antihypertensive medications.

Table 3. Crude and adjusted HRs of cardiovascular death and all-cause mortality associated with normalised blood pressure in older adults with or without HF (time-dependent analysis*)

Groups	Number of events	Person-years	Incidence rate [c]	Crude HR (95% CI)	Adjusted HR[d] (95% CI)	*P* value for interaction
Cardiovascular death						
Heart failure						
Non-normalised BP[a]	56	1,721	3.3	Reference	Reference	
Normalised BP[b]	80	1,546	5.3	1.57 (1.12–2.21)	1.79 (1.23–2.61)	
No heart failure						0.214
Non-normalised BP[a]	80	4,696	1.7	Reference	Reference	
Normalised BP[b]	65	2,801	2.3	1.30 (0.93–1.80)	1.23 (0.87– 1.74)	
All-cause mortality						
Heart failure						
Non-normalised BP[a]	128	1,751	7.3	Reference	Reference	
Normalised BP[b]	167	1,567	10.7	1.44 (1.14–1.81)	1.48 (1.15–1.90)	
No heart failure						0.170
Non-normalised BP[a]	203	4,737	4.3	Reference	Reference	
Normalised BP[b]	157	2,833	5.5	1.26 (1.02–1.55)	1.19 (0.95–1.49)	

Abbreviations: BP, blood pressure; HR, hazard ratio; CI, confidence interval. *Time-varying exposure where each patient could contribute person-time to both exposure categories with time-dependent covariates. [a]Systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg. [b]Systolic BP < 140 mmHg and diastolic BP < 90 mmHg. [c]Per 100 person-years. [d]Adjusted for age, sex (only at baseline), BMI, smoking status, alcohol consumption, physical exercise, estimated glomerular filtration rate, albuminuria, atrial fibrillation, diabetes mellitus, hyperlipidemia, albuminuria, prior myocardial infarction, prior stroke, chronic obstructive pulmonary disease, cancer, duration of treated arterial hypertension (only at baseline) and overall number of antihypertensive medications.

regardless of age [12]. Importantly, these recommendations are based on expert consensus and extrapolation from non-HF populations, given the absence of RCTs in the area [12]. Indeed, symptomatic or pharmacologically treated HF was an explicit exclusion criterion both in HYVET [14] and the elderly specific subgroup analysis of SPRINT [15], the two largest trials to date evaluating the efficacy of BP control on mortality in older populations.

We did not observe a decreased risk of mortality associated with normalised BP in older HF patients and even observed an increased risk in the time-dependent analyses. Thus, our results do not support current recommendations. Some pathophysiological considerations regarding our findings need to be mentioned. First, since impaired BP homeostasis is not uncommon in advanced age, normalising BP in older patients may limit their capacity to preserve vital organ perfusion, potentially balancing out the beneficial effects of antihypertensive drugs [26]. Also based on BIS data, we recently observed an increased mortality risk associated with normalised BP in older patients treated with antihypertensive drugs, an effect driven by subgroups where BP homeostasis is likely even more compromised than in the

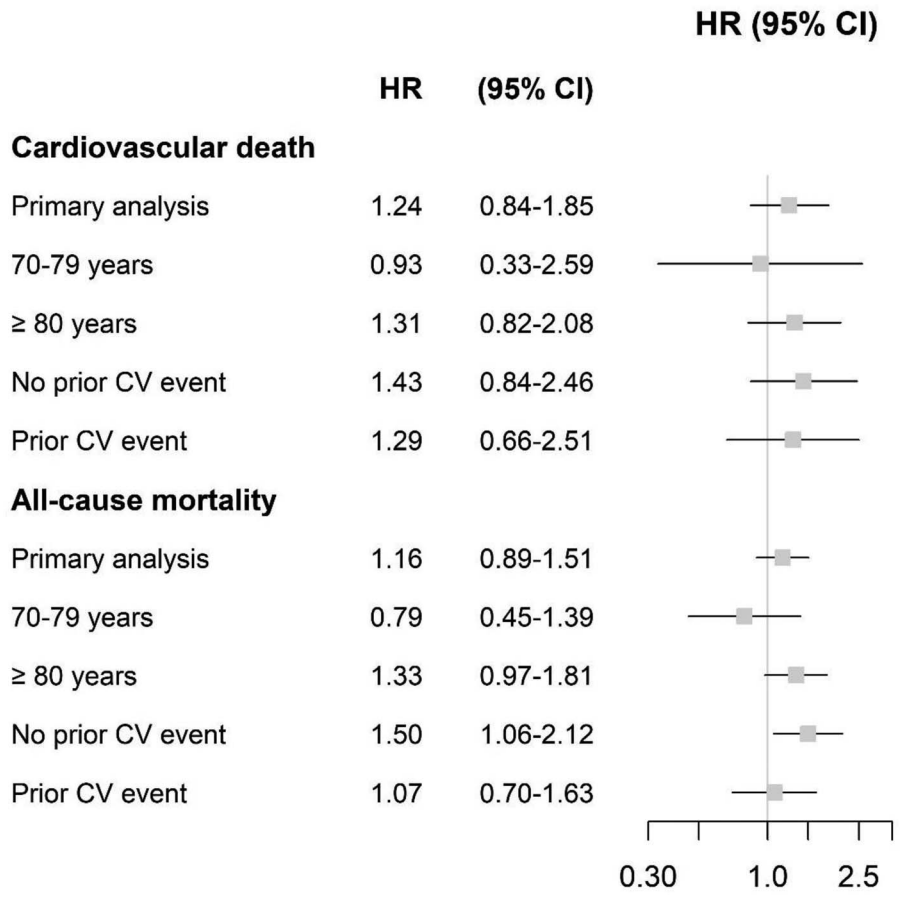

Figure 2. Forest plot summarising the results (adjusted HRs of cardiovascular death and all-cause mortality associated with normalised blood pressure) of the primary analysis and the secondary analyses in older patients with HF ($n = 544$). Abbreviations: HR, hazard ratio; CI, confidence interval; CV, cardiovascular.

general older population (i.e. octogenarians, patients with prior cardiovascular events) [27]. Second, given the high prevalence of frailty among older HF patients and the known association between frailty and cardiovascular morbidity and mortality [28–30], it is possible that 'conventional' therapeutic approaches established for younger, healthier populations are less effective in the setting of frail individuals.

Previous retrospective observational studies have also suggested an association between low BP and worse clinical outcomes in older HF patients [16–18]. However, the primary data source for these studies was a registry of patients hospitalised with HF between 2003 and 2004 (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure [OPTIMIZE-HF]) [31] and followed up to 2008. Thus, the generalizability of their findings to community-dwelling older adults and to more contemporary populations is unclear. Moreover, previous studies were not able to assess long-term effects of BP control (longest median follow-up 2.3 years) [16]. Finally, no information on cause of death was provided.

Our study has several strengths. First, using a population-based design and applying few exclusion criteria likely maximised the generalizability of our results. Second, the median follow-up of 7.5 years allowed us to assess the long-term effects of BP control in older HF patients, filling an important knowledge gap. Third, the combination of clinical data from face-to-face interviews with administrative data provided information of great granularity. Finally, death events were ascertained from death certificates and hospital discharge notes, and adjudication of cause of death was conducted independently by three physicians; this meticulous approach likely minimised outcome misclassification, while also providing novel estimates on the risk of cardiovascular death.

Our study also has limitations. First, confounding is possible given the observational design. To mitigate this bias, we adjusted for several potential confounders including lifestyle variables and comorbidities. However, other potential confounders such as frailty were not available in our data [30]. Second, our primary analysis was time-fixed and based on BP control at cohort entry. Thus, misclassification of exposure is possible given the long follow-up. When updating BP control 'status' (and the covariates) during follow-up, we observed an increased risk of both outcomes associated with normalised BP. Thus, it is possible that an increased risk was 'diluted' in the primary, time-fixed analysis. Third, the

secondary analyses were based on relatively few events and their findings should be interpreted with caution. Fourth, given the low sensitivity of HF diagnosis in administrative data [32], some HF patients could have been misclassified as 'non-HF'. Finally, we did not have access to echocardiographic data and were thus unable to distinguish between HF with preserved and with reduced ejection fraction.

Overall, our study shows that normalised BP is not associated with a decreased risk of cardiovascular death and all-cause mortality in older HF patients. Given the scarcity of available clinical evidence in the area, these results provide much needed insight on the effectiveness of pharmacologic BP control in this vulnerable population. Moreover, they argue for individualised benefit–risk assessment in older HF patients until data from pragmatic RCTs are available.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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