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Influence of blood pressure and blood pressure change on the risk of congestive heart failure in the elderly

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Summary

Background: While elevated blood pressure (BP) has been consistently associated with incident congestive heart failure (CHF), much less is known about the effect of BP change. We therefore assessed the association of BP change over time with subsequent risk of CHF.

Methods: 4655 participants ≥65 years old from the prospective Established Populations for Epidemiologic Studies of the Elderly program who were alive and free of CHF after six years of follow-up were included. Categories of sustained high BP, sustained low BP, BP progression and BP regression were defined according to BP differences between study entry and six years of follow-up. The primary endpoint was incident CHF subsequent to the six year examination.

Results: During 4.3 years of follow-up after the six year examination, 642 events occurred. The hazard ratio (HR) (95% confidence interval (CI)) for systolic BP ≥160 compared to <120 mm Hg at six years was 1.39 (1.04–1.86). Conversely, the lowest diastolic BP category at six years was associated with an increased risk of incident CHF (HR (95% CI) <70 mm Hg versus 70–79 mm Hg 1.42 (1.18–1.71)). Systolic and diastolic BP were better predictors than pulse pressure. The HRs (95% CI) for incident CHF associated with sustained high systolic BP ≥160 mm Hg and systolic BP progression were 1.35 (0.97–1.89) and 1.45 (1.14–1.85), respectively. Conversely, significant associations were found in those with sustained low diastolic BP or diastolic BP regression (HR (95% CI) 1.42 (1.11–1.83) and 1.45 (1.19–1.76), respectively).

Conclusion: While persistently elevated systolic BP and systolic BP progression were strong predictors of CHF in the elderly, inverse associations were found with regard to diastolic BP. Systolic and diastolic BP were better predictors of CHF than pulse pressure.

Keywords: hypertension; blood pressure; pulse pressure; heart failure; mortality

Introduction

Elevated blood pressure is a powerful predictor of congestive heart failure and other cardiovascular disease outcomes. [1–3] For example, the Framingham Heart Study found that hypertension accounted for 39% and 59% of congestive heart failure cases in men and women, respectively [1]. However, although blood pressure has been associated with cardiovascular events in many studies, the relationship between blood pressure change over time and subsequent risk of cardiovascular disease has received little attention. In initially healthy women, we recently found an increased risk of myocardial infarction, stroke or cardiovascular death shortly after a diagnosis of hypertension was established [3]. Less information is available with regard to other population groups and different disease outcomes.

Several investigators have demonstrated a J-shaped relationship between cardiovascular disease and diastolic but not systolic blood pressure, suggesting that change in different blood pressure components may have a differential prognostic impact [4–6]. In this context, the J-shaped relationship between diastolic blood pressure and cardiovascular disease has been used as an explanatory link for the increased cardiovascular risk

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associated with pulse pressure, the difference between systolic and diastolic blood pressure. Many studies have in fact shown that pulse pressure is an independent predictor of stroke, coronary heart disease and congestive heart failure [7–12]. Whether pulse pressure provides independent information above systolic or diastolic blood pressure is controversial, and few studies actually compared the different blood pressure components using appropriate methods [9, 13], in particular with regard to congestive heart failure.

To address these issues, we compared the ability of systolic blood pressure, diastolic blood pressure and pulse pressure, either alone or in various combinations, to predict incident congestive heart failure. We also assessed whether blood pressure changes over time are associated with incident congestive heart failure, using data from three population based cohorts of the Established Populations for Epidemiologic Studies of the Elderly program.

Methods

Study population

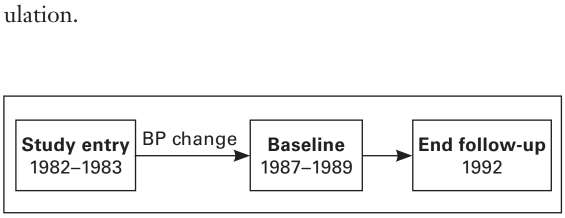
The methods of the Established populations for Epidemiologic Studies of the Elderly studies have been described in detail elsewhere [14]. The timeline for the current study is described in the figure. In brief, from 1982 to 1983, participants aged at least 65 years were recruited using population surveys in East Boston, Massachusetts, Washington and Iowa counties in Iowa, and from a stratified random sample of residents in New Haven, Connecticut. Trained interviewers conducted in-home examinations at study entry and in-house follow-up evaluations in 1984 to 1986 and 1987 to 1989. Telephone interviews were completed in other years. Baseline participation rates ranged from 80% to 85%.

Information was collected on demographic characteristics, medical history, functional abilities, and lifestyle habits. During in-home visits, interviewers also obtained information on prescription and non-prescription drugs taken in the previous two weeks, and performed blood pressure measurements [15, 16]. Prevalent conditions were assessed as previously described [8]. Participants were linked to the Medicare Provider Analysis and Review files from the Health Care Finance Administration (HCFA), which provided information on all hospital admissions and five discharge diagnoses per admission from 1985 to 1992. Using local surveillance supplemented by linkage to the National Death Index, mortality follow-up through December 1992 was complete, and 99% of death certificates were obtained and coded by a single nosologist using the *International Classification of Diseases*-9th revision (ICD-9).

All 5001 participants who were alive, free of congestive heart failure and who provided any follow-up information in 1987–1989 were eligible for this study. To define a cohort without prior congestive heart failure, we excluded participants with a previous HCFA diagnosis of congestive heart failure and those without a previous HCFA diagnosis of congestive heart failure but who were taking a combination of either digoxin and loop diuretics, or digoxin, loop diuretics and angiotensin-converting enzyme inhibitors, or who had missing information on medications. We also excluded 346 subjects with missing blood pressure information in 1987–1989, and the remaining 4655 participants constituted the final study population.

Figure 1

Study timeline.



Study variables

In East Boston and New Haven, a trained interviewer took three blood pressure measurements at 30 second intervals using a standard mercury sphygmomanometer, after the participant had been seated for at least five minutes, according to the protocol used in the Hypertension Detection and Follow-up Program [17]. Two measurements were taken in Iowa. For the present study, systolic blood pressure was the average of all systolic and diastolic blood pressure the average of all diastolic blood pressure measures. Pulse pressure was defined as systolic blood pressure minus diastolic blood pressure.

To assess the impact of blood pressure change on subsequent risk of incident heart failure, participants were categorised into the following pre-specified categories: Sustained high blood pressure was defined as systolic blood pressure, diastolic blood pressure or pulse pressure ≥160 mm Hg, ≥70 mm Hg or ≥75 mm Hg, respectively at study entry and at the 1987–1989 examination; blood pressure progression was defined as systolic blood pressure, diastolic blood pressure or pulse pressure <160 mm Hg, <70 mm Hg or <75 mm Hg, respectively at study entry and ≥160 mm Hg, ≥70 mm Hg or ≥75 mm Hg, respectively at the 1987–1989 examination; blood pressure regression was defined as systolic blood pressure, diastolic blood pressure or pulse pressure ≥160 mm Hg, ≥70 mm Hg or ≥75 mm Hg, respectively at study entry and <160 mm Hg, <70 mm Hg or <75 mm Hg, respectively at the 1987–1989 examination; sustained low blood pressure was defined as diastolic blood pressure or pulse pressure <70 mm Hg or <75 mm Hg, respectively both at study entry and at the 1987–1989 examination; sustained systolic blood pressure <160 mm Hg was defined as systolic blood pressure <160 mm Hg at both examinations. The threshold for pulse pressure was chosen as the cut-off value for the highest quartile.

Diabetes mellitus was defined by self-report, use of insulin or oral hypoglycaemic agents, or previous HCFA diagnosis. Prevalent coronary heart disease (*ICD-9* code 410-414, prior percutaneous transluminal coronary angioplasty or coronary artery bypass grafting), valvular heart disease, and atrial fibrillation were defined by HCFA diagnoses.

Outcome ascertainment

The primary endpoint for the present study was a combination of first hospitalisation for congestive heart failure, defined by ICD-9 code 428 in any of five diagnostic fields for any hospitalisation after the subject's 1987 to 1989 evaluation (n = 581), or death due to congestive heart failure as seen on the death certificate but no prior HCFA diagnosis of congestive heart failure (n = 61).

Statistical analysis

To examine the relationship between blood pressure components and risk of incident heart failure, we grouped participants into pre-specified, clinically relevant categories of systolic and diastolic blood pressure at the 1987–1989 examination: <120 mm Hg, 120–139 mm Hg, 140–159 mm Hg, and ≥160 mm Hg for systolic blood pressure, and <70 mm Hg, 70–79 mm Hg, 80–89 mm Hg, and ≥90 mm Hg for diastolic blood pressure [18]. Pulse pressure was categorised according to approximate quartiles in the study population.

We constructed Cox proportional-hazards models to calculate hazard ratios and 95% confidence intervals across blood pressure categories. All models were stratified by study site. In a first step, we fitted age and sex adjusted models. Subsequently, these models were additionally adjusted for prevalent diabetes mellitus, coronary heart disease, valvular heart disease, prior atrial fibrillation, and intake of antihypertensive therapy. We used the –2 log likelihood to compare models of different blood pressure components, either individually or in various combinations. Lower –2 log likelihood values indicate better model fit. Where appropriate, between model differences were compared using chi square tests.

Using the same approach, we then constructed Cox proportional-hazards models including indicators of categories of blood pressure change as defined above. We again used the –2 log likelihood to compare different models of blood pressure change. To assess whether the intake of antihypertensive therapy modifies the effect of blood pressure change on incident heart failure, participants were stratified according to their intake or not of antihypertensive treatment. The impact of blood pressure change on incident heart failure was assessed separately in the two strata. Blood pressure change by antihypertensive treatment interaction tests were performed in the non-stratified models using likelihood ratio tests.

Categorical variables were entered in the Cox models using binary indicator variables. The proportional hazards assumption was examined for all models by including a blood pressure category by logarithm of time interaction into the model. [19] No violations for this assumption were found. All analyses were carried out using SAS version 9 (SAS Institute Inc, Cary, NC). A two-tailed p value <0.05 was considered to indicate statistical significance.

Table 1

Baseline characteristics.

	East Boston (n = 1621)	Iowa (n = 1812)	New Haven (n = 1222)
Age, years	78 ± 5	79 ± 5	79 ± 6
Women, %	66.1	65.9	63.7
Systolic blood pressure, mm Hg	137 ± 19	141 ± 19	138 ± 19
Diastolic blood pressure, mm Hg	75 ± 10	73 ± 10	76 ± 11
Pulse pressure, mm Hg	62 ± 17	67 ± 17	62 ± 16
Use of antihypertensive drugs, %	45.7	37.0	41.5
Diabetes mellitus, %	18.8	13.5	16.4
Coronary heart disease, %	10.5	6.6	10.5
Atrial fibrillation, %	2.8	2.5	2.3
Valvular heart disease, %	1.7	1.7	1.1

Data are mean ± standard deviation or percentages

Table 2

Age-adjusted incidence rates across blood pressure categories.

Blood pressure component	Category 1	Category 2	Category 3	Category 4
Systolic blood pressure	<120	120–139	140–159	≥160
Events/person-years	79/2304	263/7437	182/5661	118/2252
Age-adjusted incidence rate*	36.6	37.3	32.8	51.4
Diastolic blood pressure	<70	70–79	80–89	≥90
Events/person-years	239/5037	208/6871	145/4400	50/1346
Age-adjusted incidence rate*	45.6	31.7	35.1	40.5
Pulse pressure	<53	53–62	63–74	≥75
Events/person-years	141/4535	134/4605	167/4383	200/4130
Age-adjusted incidence rate*	34.7	31.0	38.7	46.3

* Events per 1000 person-years of follow-up

Results

Baseline characteristics according to study site are shown in table 1. In the combined group, mean age was 79 ± 6 years, systolic blood pressure 139 ± 19 mm Hg, diastolic blood pressure 75 ± 10 mm Hg and pulse pressure 64 ± 17 mm Hg.

During a median (interquartile range) follow-up of 4.3 (3.6–4.7) years, 642 primary outcome events occurred among 4655 study participants. Event rates across blood pressure categories are shown in table 2. A systolic blood pressure ≥160 mm Hg was associated with a substantially higher risk compared with lower systolic blood pressure values (51.4 versus 32.8–37.3 events per 1000 person-years). Across categories of diastolic blood pressure we found a J-shaped relationship with incident heart failure, participants in the lowest diastolic blood pressure having the highest risk (45.6 events per 1000 person-years) (table 2). Across categories of pulse pressure the highest rates of incident heart failure occurred in the two highest quartiles.

Multivariable adjustment confirmed these relationships (table 3). Participants with a systolic blood pressure ≥160 mm Hg had a 39% increased risk of incident heart failure compared to those <120 mm Hg, whereas in those with moderately elevated systolic blood pressure the risk of heart failure was not increased. While the increased risk in individuals with diastolic blood pressure ≥90 mm Hg became non-significant after multivariable adjustment, participants with diastolic blood pressure <70 mm Hg had a 42% increased risk compared to those with a diastolic blood pressure between 70 and 79 mm Hg (p = 0.0003). Finally, participants in the highest quartile of pulse pressure had a significantly increased risk of incident heart failure compared to those in the lowest quartile (hazard ratio (95% confidence interval) 1.28 (1.02–1.59)). As indicated by a lower –2 log likelihood, both systolic and diastolic blood pressure provided a better model fit compared to pulse pressure after multivariable adjustment (table 3).

Adding systolic and diastolic blood pressure in the same multivariable model strengthened the associations described above (table 3). In the joint model, the hazard ratios (95% confidence intervals) for systolic blood pressure ≥160 mm Hg and diastolic blood pressure <70 mm Hg were 1.61 (1.17–2.20) and 1.46 (1.20–1.76), respectively. Consequently, the joint model provided a significantly better model fit compared to either model alone (p = 0.002 for both comparisons). On the other hand, adding categories of diastolic blood pressure and pulse pressure in the same model slightly attenuated the relationship between pulse pressure and incident heart failure (table 3). The association between diastolic blood pressure and incident heart failure remained almost unchanged after adjustment for pulse pressure (Data not shown). While the joint model significantly improved both individual models (p = 0.005 for pulse pressure only model, p = 0.04 for diastolic blood pressure only model), the joint diastolic/pulse

Table 3

Relative risk of congestive heart failure across blood pressure categories.

Blood pressure component	Category 1	Category 2	Category 3	Category 4	-2 log likelihood
Systolic blood pressure	<120	120–139	140–159	≥160	–
Age/sex adjusted	Referent	1.05 (0.82–1.35)	0.95 (0.73–1.23)	1.53 (1.15–2.03)	9007.3
Multivariable model*	Referent	1.08 (0.84–1.39)	0.90 (0.69–1.17)	1.39 (1.04–1.86)	8896.5
Combined model†	Referent	1.17 (0.91–1.52)	1.02 (0.77–1.35)	1.61 (1.17–2.20)	8881.4
Diastolic blood pressure	<70	70–79	80–89	≥90	–
Age/sex adjusted	1.47 (1.22–1.77)	Referent	1.14 (0.92–1.41)	1.32 (0.97–1.80)	9006.8
Multivariable model*	1.42 (1.18–1.71)	Referent	1.16 (0.93–1.43)	1.26 (0.93–1.73)	8896.0
Combined model†	1.46 (1.20–1.76)	Referent	1.11 (0.90–1.38)	1.09 (0.78–1.51)	8881.4
Pulse pressure	<53	53–62	63–74	≥75	
Age/sex adjusted	Referent	0.92 (0.73–1.16)	1.18 (0.95–1.48)	1.44 (1.16–1.79)	9005.0
Multivariable model*	Referent	0.91 (0.72–1.16)	1.11 (0.88–1.39)	1.28 (1.02–1.59)	8900.1
Combined model‡	Referent	0.91 (0.72–1.15)	1.09 (0.87–1.37)	1.25 (1.00–1.56)	8887.4

Data are hazard ratio (95% confidence interval)

* Adjusted for age, sex, history of diabetes mellitus, coronary heart disease or valvular heart disease, prior atrial fibrillation, and antihypertensive drug intake

† Combined multivariable model for systolic and diastolic blood pressure

‡ Combined multivariable model for diastolic blood pressure and pulse pressure

Table 4

Risk of congestive heart failure according to blood pressure change.

Blood pressure component	Sustained low BP	BP regression	BP progression	Sustained high BP	-2 log L
Systolic blood pressure	N = 3499	N = 539	N = 422	N = 195	
Age/sex adjusted	Referent	1.19 (0.94–1.50)	1.57 (1.23–1.99)	1.55 (1.11–2.16)	9006.5
Multivariable model*	Referent	1.07 (0.85–1.36)	1.45 (1.14–1.85)	1.35 (0.97–1.89)	8899.5
Combined model 1†	Referent	1.11 (0.87–1.41)	1.57 (1.23–2.01)	1.47 (1.05–2.07)	8883.2
Diastolic blood pressure	N = 498	N = 861	N = 618	N = 2678	
Age/sex adjusted	1.37 (1.08–1.75)	1.40 (1.15–1.70)	1.10 (0.86–1.41)	Referent	9009.7
Multivariable model*	1.34 (1.05–1.71)	1.36 (1.12–1.65)	1.13 (0.88–1.44)	Referent	8898.1
Combined model 1†	1.42 (1.11–1.83)	1.45 (1.19–1.76)	1.13 (0.88–1.44)	Referent	8883.2
Combined model 2‡	1.32 (1.03–1.68)	1.35 (1.11–1.64)	1.11 (0.87–1.41)	Referent	8889.6
Pulse pressure	N = 2455	N = 636	N = 1158	N = 406	
Age/sex adjusted	Referent	1.27 (1.02–1.59)	1.48 (1.20–1.82)	1.46 (1.14–1.88)	9005.8
Multivariable model 1*	Referent	1.18 (0.95–1.48)	1.36 (1.10–1.68)	1.26 (0.97–1.62)	8900.4
Combined model 2‡	Referent	1.16 (0.93–1.45)	1.35 (1.10–1.67)	1.21 (0.94–1.57)	8889.6

Data are hazard ratio (95% confidence interval)

BP: Blood pressure; L: Likelihood

Sustained low was defined as systolic BP, diastolic BP or pulse pressure <160 mm Hg, <70 mm Hg or <75 mm Hg, respectively at study entry and after six years of follow-up; BP regression was defined as systolic BP, diastolic BP or pulse pressure ≥160 mm Hg, ≥70 mm Hg or ≥75 mm Hg, respectively at study entry and <160 mm Hg, <70 mm Hg or <75 mm Hg, respectively after six years of follow-up; BP progression was defined as systolic BP, diastolic BP or pulse pressure <160 mm Hg, <70 mm Hg or <75 mm Hg, respectively at study entry and ≥160 mm Hg, ≥70 mm Hg or ≥75 mm Hg, respectively after six years of follow-up; Sustained high BP was defined as systolic BP, diastolic BP or pulse pressure ≥160 mm Hg, ≥70 mm Hg or ≥75 mm Hg, respectively at study entry and after six years of follow-up.

* Adjusted for age, sex, history of diabetes mellitus, coronary heart disease or valvular heart disease, prior atrial fibrillation, and antihypertensive drug intake

† Combined multivariable model including change variables for systolic blood pressure and diastolic blood pressure

‡ Combined multivariable model including change variables for diastolic blood pressure and pulse pressure

Table 5

Risk of congestive heart failure according to blood pressure change, stratified by antihypertensive therapy at baseline.

Blood pressure component	Sustained low BP	BP regression	BP progression	Sustained high BP	-2 log L
Systolic blood pressure					
No antihypertensive drugs (N = 2737)	Referent	1.02 (0.70–1.48)	1.78 (1.27–2.49)	1.57 (0.89–2.74)	4183.3
Antihypertensive drugs (N = 1918)	Referent	1.09 (0.80–1.48)	1.17 (0.83–1.66)	1.23 (0.81–1.88)	3828.6
Diastolic blood pressure					
No antihypertensive drugs (N = 2737)	1.45 (1.09–1.92)	1.58 (1.15–2.17)	1.23 (0.89–1.71)	Referent	4184.1
Antihypertensive drugs (N = 1918)	1.09 (0.73–1.62)	1.29 (0.98–1.70)	1.05 (0.72–1.52)	Referent	3826.9
Pulse pressure					
No antihypertensive drugs (N = 2737)	Referent	0.98 (0.70–1.38)	1.38 (1.03–1.84)	1.34 (0.92–1.94)	4188.9
Antihypertensive drugs (N = 1918)	Referent	1.36 (1.01–1.83)	1.33 (0.98–1.80)	1.19 (0.84–1.70)	3824.5

Data are hazard ratio (95% confidence interval). BP: Blood pressure. Categories as described in table 4. All models are adjusted for age, sex, history of diabetes mellitus, coronary heart disease or valvular heart disease, prior atrial fibrillation, and antihypertensive drug intake.

pressure model had a higher –2 Log likelihood compared to the joint systolic/diastolic blood pressure model (8887.4 versus 8881.4), indicating that the latter provides more information with regard to incident heart failure.

Several measures of blood pressure change were associated with incident heart failure. As shown in table 4, participants with systolic blood pressure progression between study entry and the 1987–1989 examination had a significantly increased risk of incident heart failure thereafter compared to those with sustained systolic blood pressure <160 mm Hg (hazard ratio (95% confidence interval) after multivariable adjustment 1.45 (1.14–1.85)). The association between persistently elevated systolic blood pressure and incident heart failure was of borderline statistical significance (hazard ratio (95% confidence interval) 1.35 (0.97–1.89), p = 0.08). Conversely, significant associations were found in participants who experienced sustained low diastolic blood pressure or diastolic blood pressure regression (hazard ratio (95% confidence interval) for incident heart failure 1.34 (1.05–1.71) and 1.36 (1.12–1.65), respectively). Accordingly, an increase in pulse pressure during follow-up was associated with a significant 36% increase in risk compared to a sustained low pulse pressure (p = 0.005).

Adding change variables for systolic and diastolic blood pressure to the same model strengthened the associations for measures of change in both systolic and diastolic blood pressure (table 4, combined model 1). Accordingly, model fit significantly improved compared to either individual model (p = 0.001 compared to the systolic and p = 0.002 compared to the diastolic blood pressure model). Adding change variables for diastolic blood pressure to the pulse pressure change model did not induce major changes in the risk estimates for diastolic blood pressure or pulse pressure, but significantly improved model fit compared to the pulse pressure only model (p = 0.01) and the diastolic blood pressure only model (p = 0.04). Nevertheless, the joint systolic and diastolic blood pressure change model provided better fit compared to the joint diastolic blood pressure and pulse pressure change model, as indicated by the lower –2 Log likelihood (8883.2 versus 8889.6).

The impact of blood pressure change after stratification according to antihypertensive therapy is shown in table 5. High systolic blood pressure and systolic blood pressure progression were independent predictors of incident heart failure in participants not on antihypertensive treatment. However, in those taking antihypertensive treatment, none of the systolic blood pressure change variables was independently related to incident heart failure. Sustained low diastolic blood pressure was an independent predictor of heart failure in participants not taking antihypertensive treatment, but not in those who were taking antihypertensive treatment (hazard ratio (95% confidence interval) 1.09 (0.73–1.62)). However, none of the antihypertensive treatment by blood pressure change interaction terms was statistically significant (p >0.36 for all comparisons).

Discussion

In the present study we found evidence that in elderly individuals, different components of blood pressure change had differing associations with the risk of incident congestive heart failure. While a systolic blood pressure that persisted at levels ≥160 mm Hg and systolic blood pressure progression over six years to levels ≥160 mm Hg were powerful indicators of risk, inverse associations were found with regard to diastolic blood pressure. Both sustained low diastolic blood pressure <70 mm Hg and diastolic blood pressure regression to levels <70 mm Hg were independently associated with incident heart failure. In a combined model including both systolic and diastolic blood pressure categories, the associations for high systolic and low diastolic blood pressure became even stronger, suggesting that both components provide incremental information. These findings have recently been found for a much broader endpoint [20]. Accordingly, we found a significant relationship between pulse pressure progression and incident heart failure.

The second major finding of this study was that baseline systolic and diastolic blood pressure were better predictors of incident congestive heart failure than pulse pressure. Although we confirmed findings from previous studies that all three blood pressure components significantly predict incident heart failure after multivariable adjustment [8, 10, 13, 21, 22], both systolic and diastolic blood pressure alone provided better model fit compared with pulse pressure. Thus, in contrast to previous findings, our data suggest that pulse pressure does not provide incremental information for the prediction of heart failure in elderly individuals.

Several reasons may be implicated with regard to these differential findings. Pathophysiologically, pulse pressure is considered to be an indicator of conduit vessel stiffness associated with an increase in wave reflection amplitude [23, 24]. As after the age of 60 years, systolic blood pressure increases and diastolic blood pressure falls [25], pulse pressure substantially increases, potentially explaining the superiority of pulse pressure over systolic and diastolic blood pressure in some studies [9, 11]. However, as suggested in the present study, this may not be true for other outcomes and/or population groups [13]. Pulse pressure, calculated as a linear combination between systolic and diastolic blood pressure, may not fully capture the nonlinear association between diastolic but not systolic blood pressure and incident heart failure. In this context, diastolic blood pressure regression may be a better indicator of aortic stiffness and progressive vascular damage in this population group.

An alternative explanation for our findings may be that in elderly subjects, mechanisms other than increased pulse pressure and vessel stiffness are strongly involved in the pathogenesis of congestive heart failure. For example, the high prevalence of diastolic dysfunction in the elderly [26] may make this population group susceptible to small increases of systolic blood pressure. Therefore, systolic blood pressure may be a better predictor than pulse pressure. Interestingly, in younger individuals free of coronary heart disease and not taking antihypertensive therapy, the association between pulse pressure and incident heart failure seemed to be similar to that with systolic blood pressure [10], suggesting that the predictive ability of pulse pressure may vary according to the characteristics of the population studied. Similar differences across population groups have been shown in prior studies with regard to the association of systolic and diastolic blood pressure with coronary heart disease [27, 28].

In the present study we found an increased risk of incident heart failure associated with elevated systolic blood pressure and systolic blood pressure progression, underscoring the potential importance of blood pressure control in the very elderly. In this context it is interesting to note that participants of this study who were taking antihypertensive treatment and who had a sustained low diastolic blood pressure <70 mm Hg did not have an increased risk of heart failure (hazard ratio (95% confidence interval) 1.09 (0.73–1.62). Although this subgroup analysis has to be interpreted with caution, it may nevertheless indicate that lowering diastolic blood pressure below 70 mm Hg using medical therapy does not increase the risk of heart failure.

An important strength of this study represents its focus on blood pressure change and subsequent risk of congestive heart failure. The present study should be interpreted in the context of its limitations. Firstly, we included only elderly individuals from the United States and our findings should not be extrapolated to other populations or different disease outcomes. Secondly, only hospitalisations for heart failure were assessed in this study and this classification may have missed some outpatient cases. However, given the progressive nature of congestive heart failure, most patients with heart failure require hospitalisation at some point in their disease. Thirdly, study participants were recruited in the 1980s and the applicability of our results to a contemporary patient population is uncertain. Over the last 20 years, major progress has been made in the treatment of patients with hypertension, and guidelines have adopted different treatment threshold over time. On the other hand, our results are still of interest from a pathophysiological perspective. In fact, we might have obtained a much cleaner impression on the relationship between blood pressure and incident congestive heart failure, because in the current study fewer patients were on blood pressure lowering treatment compared to a more recent sample. Finally, undiagnosed left ventricular dysfunction at baseline in some participants may have influenced their baseline blood pressure levels. As subclinical left ventricular dysfunction also predisposes to the development of overt heart failure, this may have slightly distorted the strength of some blood pressure endpoint associations.

In conclusion, in this study we found a significant relationship of persistently elevated systolic blood pressure and systolic blood pressure progression with incident congestive heart failure in a community based elderly population sample. Thus, our study provides indirect evidence that tight blood pressure control is beneficial even in the very elderly. We also found that low diastolic blood pressure and diastolic blood pressure regression are significantly associated with congestive heart failure risk. Although diastolic blood pressure provided additional prognostic information independent of systolic blood pressure, our study did not indicate superior risk prediction with pulse pressure compared with either systolic or diastolic blood pressure alone.

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References

1 Levy D, Larson MG, Vasan RS, Kannel WB, Ho KK. The progression from hypertension to congestive heart failure. JAMA. 1996;275:1557–62.
2 Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360:1903–13.
3 Conen D, Ridker PM, Buring JE, Glynn RJ. Risk of cardiovascular events among women with high normal blood pressure or blood pressure progression: prospective cohort study. BMJ. 2007;335:432.
4 Farnett L, Mulrow CD, Linn WD, Lucey CR, Tuley MR. The J-curve phenomenon and the treatment of hypertension. Is there a point beyond which pressure reduction is dangerous? JAMA. 1991;265:489–95.
5 Cruickshank JM, Thorp JM, Zacharias FJ. Benefits and potential harm of lowering high blood pressure. Lancet. 1987;1:581–4.
6 Samuelsson O, Wilhelmsen L, Andersson OK, Pennert K, Berglund G. Cardiovascular morbidity in relation to change in blood pressure and serum cholesterol levels in treated hypertension. Results from the primary prevention trial in Goteborg, Sweden. JAMA. 1987;258:1768–76.
7 Assmann G, Cullen P, Evers T, Petzinna D, Schulte H. Importance of arterial pulse pressure as a predictor of coronary heart disease risk in PROCAM. Eur Heart J. 2005;26:2120–6.
8 Chae CU, Pfeffer MA, Glynn RJ, Mitchell GF, Taylor JO, Hennekens CH. Increased pulse pressure and risk of heart failure in the elderly. JAMA. 1999;281:634–9.
9 Glynn RJ, Chae CU, Guralnik JM, Taylor JO, Hennekens CH. Pulse pressure and mortality in older people. Arch Intern Med. 2000;160:2765–72.
10 Haider AW, Larson MG, Franklin SS, Levy D. Systolic blood pressure, diastolic blood pressure, and pulse pressure as predictors of risk for congestive heart failure in the Framingham Heart Study. Ann Intern Med. 2003;138:10–6.
11 Franklin SS, Khan SA, Wong ND, Larson MG, Levy D. Is pulse pressure useful in predicting risk for coronary heart Disease? The Framingham heart study. Circulation. 1999;100:354–60.
12 Nair GV, Chaput LA, Vittinghoff E, Herrington DM. Pulse pressure and cardiovascular events in postmenopausal women with coronary heart disease. Chest. 2005;127:1498–506.
13 Mosley WJ, 2nd, Greenland P, Garside DB, Lloyd-Jones DM. Predictive utility of pulse pressure and other blood pressure measures for cardiovascular outcomes. Hypertension. 2007;49:1256–64.
14 Cornoni-Huntley J, Ostfeld AM, Taylor JO, et al. Established populations for epidemiologic studies of the elderly: study design and methodology. Aging (Milano). 1993;5:27–37.
15 Cornoni-Huntley J, Brock DB, Ostfeld AM, Taylor JO, Wallace RM. Established populations for Epidemiologic Studies of the Elderly: Resource Data Book. Bethesda, Md:National Institute of Health. 1986: NIH publication 86-2443.
16 Glynn RJ, Field TS, Satterfield S, et al. Modification of increasing systolic blood pressure in the elderly during the 1980s. Am J Epidemiol. 1993;138:365–79.
17 Hypertension Detection and Follow-up Program Cooperative Group. Variability of blood pressure and the results of screening in the hypertension detection and follow-up program. J Chronic Dis. 1978;31:651–67.
18 The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Arch Intern Med. 1997;157:2413–46.
19 Cox DR. Regression models and life tables. J Roy Stat Soc B. 1972;34:187–220.
20 Franklin SS, Lopez VA, Wong ND, et al. Single versus combined blood pressure components and risk for cardiovascular disease: the Framingham Heart Study. Circulation. 2009; 119:243–50.
21 Vaccarino V, Holford TR, Krumholz HM. Pulse pressure and risk for myocardial infarction and heart failure in the elderly. J Am Coll Cardiol. 2000;36:130–8.
22 Kostis JB, Lawrence-Nelson J, Ranjan R, Wilson AC, Kostis WJ, Lacy CR. Association of increased pulse pressure with the development of heart failure in SHEP. Systolic Hypertension in the Elderly (SHEP) Cooperative Research Group. Am J Hypertens. 2001;14:798–803.
23 Dart AM, Kingwell BA. Pulse pressure – a review of mechanisms and clinical relevance. J Am Coll Cardiol. 2001;37:975–84.
24 Nichols WW, Nicolini FA, Pepine CJ. Determinants of isolated systolic hypertension in the elderly. J Hypertens Suppl. 1992;10:S73–7.
25 Burt VL, Whelton P, Roccella EJ, et al. Prevalence of hypertension in the US adult population. Results from the Third National Health and Nutrition Examination Survey, 1988–1991. Hypertension. 1995;25:305–13.
26 Zile MR, Brutsaert DL. New concepts in diastolic dysfunction and diastolic heart failure: Part I: diagnosis, prognosis, and measurements of diastolic function. Circulation. 2002;105:1387–93.
27 Franklin SS, Larson MG, Khan SA, et al. Does the relation of blood pressure to coronary heart disease risk change with aging? The Framingham Heart Study. Circulation. 2001;103:1245–9.
28 Lichtenstein MJ, Shipley MJ, Rose G. Systolic and diastolic blood pressures as predictors of coronary heart disease mortality in the Whitehall study. Br Med J (Clin Res Ed). 1985; 291:243–5.