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Systolic-Diastolic Hypertension versus Isolated Systolic Hypertension and Incident Heart Failure in Older Adults: Insights from the Cardiovascular Health Study

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Abstract

Background—Isolated systolic hypertension (ISH) is common in older adults and is a risk factor for incident heart failure (HF). We examined the association of systolic-diastolic hypertension (SDH) with incident HF and other outcomes in older adults.

Methods—In the Cardiovascular Health Study (CHS), 5776 community-dwelling adults ≥65 years had data on baseline systolic and diastolic blood pressure (SBP and DBP). We excluded those with DBP <60 mm Hg (n=821), DBP ≥90 and SBP <140 mm Hg (n=28), normal BP, taking anti-hypertensive drugs (n=1138), normal BP, not taking anti-hypertensive drugs, history of hypertension (n=193), and baseline HF (n=101). Of the remaining 3495, 1838 had ISH (SBP ≥140

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and DBP <90 mm Hg) and 240 had SDH (SBP ≥140 and DBP ≥90 mm Hg). The main outcome was centrally-adjudicated incident HF over 13 years of follow-up.

Results—Participants had a mean (±SD) age of 73 (±6) years, 57% were women, and 16% African American. Incident HF occurred in 25%, 22% and 11% of participants with ISH, SDH and no hypertension, respectively. Compared to no hypertension, multivariable-adjusted hazard ratios (HR) and 95% confidence intervals (CI) for incident HF associated with ISH and SDH were 1.86 (1.51–2.30) and 1.73 (1.23–2.42), respectively. Cardiovascular mortality occurred in 22%, 24% and 9% of those with ISH, SDH and no hypertension, respectively with respective multivariable-adjusted HRs (95% CIs) of 1.88 (1.49–2.37) and 2.30 (1.64–3.24).

Conclusion—Among older adults with hypertension, both SDH and ISH have similar associations with incident HF and cardiovascular mortality.

Keywords

Isolated Diastolic Hypertension; Systolic-Diastolic Hypertension; Incident Heart Failure; Mortality

1. Introduction

Isolated systolic hypertension (ISH), an elevated systolic blood pressure (SBP) with a normal or low diastolic blood pressure (DBP), is the more common type of hypertension among older adults, and has been shown to be associated with a higher risk of incident heart failure (HF).[1] In contrast, hypertension due to elevation of both SBP and DBP is less common in older adults, and relatively less is known about the impact of systolic-diastolic hypertension (SDH) on incident HF and other cardiovascular outcomes in this population. Even less in know about the association of SDH with other cardiovascular events in this population. In the current study, we studied the association of ISH and SDH with incident HF and other outcomes among older adults in the Cardiovascular Health Study (CHS).

2. Materials and Methods

2.1. Study design and participants

The CHS is a prospective population-based longitudinal observational study of risk factors for cardiovascular disease in older adults.[2] Funded by the National Heart, Lung, and Blood Institute (NHLBI), the CHS recruited 5888 community-dwelling adults age ≥65 years from Forsyth County, North Carolina, Sacramento County, California, Washington County, Maryland, and Pittsburgh, Pennsylvania. Recruitment occurred in two phases: 5201 participants were recruited between 1989 and 1990 in the first phase and 687 African American participants were later recruited between 1992 and 1993 in the second phase to improve the generalizability of outcomes and the representation of minorities in the study.[3–5] The current analysis is based on a public-use copy of the de-identified CHS data obtained from NHLBI that included data on 5795 participants (93 participants did not consent to be part of the public-use data).[6,7]

After excluding participants without data on baseline blood pressure (n=19), those with DBP <60 mmHg (n=821), isolated diastolic hypertension (DBP ≥90 mmHg and SBP<140 mmHg; n=28), and well controlled hypertension (SBP <140 mmHg and DBP < 90 mmHg while taking antihypertensive medications, or with a prior history of hypertension; n=1331), the final sample size included 3596 participants (Figure 1). Because our primary outcome was incident HF, we also excluded 101 participants who had HF at baseline, resulting in a final cohort size of 3495 individuals.

2.2. ISH, SDH, and other baseline measurements

A random-zero sphygmomanometer was used to measure the seated blood pressure and the average of two measurements were used for both SBP and DBP.[1,8] ISH was defined as SBP ≥140 mmHg and DBP <90 mmHg and SDH was defined as SBP ≥140mmHg and DBP ≥90 mmHg.[1] The final study cohort included 3495 participants with ISH (n=1838; 53%), SDH (n=240; 7% or 12% of 2078 with hypertension) and no hypertension (n=1417; 40%). Extensive data on sociodemographic, clinical, subclinical, and laboratory variables were collected. Missing values were replaced with imputed values predicted by age, sex and race.

2.3. Outcome measures

The primary outcome of this study was incident HF during 13 years of follow-up. Incident HF was assessed by individual reports and according to the diagnosis of their physicians in semiannual visits.[9,10] To further clarify the diagnosis of HF, the CHS Events Committee examined medical charts for symptoms, physical signs, common HF medications, and follow-up appointments, which contributed to the diagnosis of HF. Secondary outcomes included all-cause, cardiovascular, and non-cardiovascular mortalities, and incident acute myocardial infarction (AMI), angina pectoris, stroke, transient ischemic attack (TIA), peripheral arterial disease (PAD), and coronary artery bypass graft (CABG) surgery. All outcomes were centrally adjudicated and the validity of this method has been well established.[1,8–10]

2.4. Statistical analysis

Baseline characteristics were compared using Pearson Chi-square and analysis of variance tests. Age-sex-race-adjusted and multivariable-adjusted Cox proportional hazard models were used to examine associations of ISH and SDH with outcomes, using no hypertension as a reference group and expressed as hazard ratios (HR) and 95% confidence intervals (CI). Log minus log survival plots were used to check for assumptions of proportional hazards. In addition to age, sex, and race, the multivariable model was also adjusted for education, income, alcohol, smoking, body mass index, prior acute myocardial infarction, diabetes, stroke, atrial fibrillation, left ventricular hypertrophy, left ventricular systolic dysfunction, serum creatinine, serum C-reactive protein, ACE inhibitors, beta-blockers, calcium channel blockers, loop diuretics, thiazide diuretics, and time to walk 15 feet. Participants with baseline AMI, angina pectoris, stroke, TIA, PAD, and CABG were excluded from analysis of their incident events. All statistical tests were 2-tailed with 95% confidence levels and P values of <0.05 were considered significant. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY was used for data analyses.

3. Results

3.1. Baseline characteristics

Overall, study participants had a mean age 73 (SD ±6) years, 57% were women and 16% were African American. Patients with ISH were older than those with SDH, who in turn were older than those with normal BP (Table 1). There were more women among those with ISH, while there were more men among those with SDH, and a third of those with SDH were African American (Table 1). Other baseline characteristics for the three study groups are presented in Table 1.

3.2. Association of ISH and SDH with incident HF

Incident HF occurred in 25%, 22% and 11% of the participants with ISH, SDH, and no hypertension, respectively (Table 2). Compared with those with normal BP, age-sex-race-adjusted HRs (95% CIs) for incident HF associated with ISH and SDH were 2.40 (1.99–2.88) and 2.19 (1.60–3.00), respectively (Table 2 and Figure 2). Both associations were attenuated after additional adjustment in the multivariable model, but remained statistically significant (Table 2).

Compared with ISH, age-sex-race-adjusted and multivariable-adjusted HRs (95% CIs) for incident HF associated with SDH were 0.92 (0.69–1.22) and 0.93 (0.69–1.24), respectively

3.3. Association of ISH and SDH with mortality

All-cause mortality occurred in 49%, 50% and 34% of the participants with ISH, SDH, and no hypertension, respectively (Table 3). Compared with those with no hypertension, age-sex-race-adjusted HRs (95% CIs) for all-cause mortality associated with ISH and SDH were 1.41 (1.25–1.57) and 1.58 (1.29–1.93), respectively (Table 3 and Figure 3). These associations remained statistically significant albeit attenuated after additional multivariable adjustment (Table 3). Associations with cardiovascular and non-cardiovascular mortalities are displayed in Table 3.

Compared with ISH, age-sex-race-adjusted and multivariable-adjusted HRs (95% CIs) for all-cause mortality associated with SDH were 1.11 (0.92–1.35) and 1.17 (0.97–1.43), respectively. Respective HRs (95% CIs) for cardiovascular mortality were 1.18 (0.89–1.56) and 1.22 (0.92–1.63), respectively.

3.4. Association of ISH and SDH with other outcomes

Acute myocardial infraction (AMI) occurred in 12%, 16% and 8% of the participants with ISH, SDH and no hypertension, respectively. Compared with those with no hypertension, age-sex-race-adjusted HRs (95% CIs) for AMI associated with ISH and SDH were 1.82 (1.45–2.29); $p<0.001$ and 2.35 (1.60–3.31); $p<0.001$ respectively Table 4. Incident stroke occurred in 18%, 19% and 8% of participants with ISH, SDH and no hypertension, respectively, with respective age-sex-race-adjusted HRs (95% CIs) of 2.40 (1.92–2.98) and 2.77 (1.95–3.93). These associations remained statistically significant after multivariable adjustment (Table 4). Associations of ISH and SDH with incidence of angina, TIA, PAD and CABG are demonstrated on Table 4.

4. Discussion

Findings from this prospective population-based study of community-dwelling older adults demonstrate that SDH, the less prevalent form of hypertension is associated with a risk of incident HF that is similar to that of ISH, the more common form of hypertension in that population. We also demonstrated that both forms of hypertension are associated with a higher risk of death in older adults, although the association appeared to be stronger with SDH. Both forms of hypertension also had similar associations with other cardiovascular events including incident AMI and stroke. To the best of our knowledge this is the first study to examine the association of SDH with cardiovascular outcomes in older adults. These findings are important as the rather similar risk profile of SDH and ISH in community-dwelling older adults suggest that both forms of hypertension need to be treated to reduce the risk of HF and other adverse cardiovascular outcomes and death in this population.

Aging is associated with arteriosclerotic stiffening of large capacitance vessels resulting in an elevation of SBP with a normal or decreased DBP and an associated widening of the pulse pressure.[11] Thus, a higher risk of incident HF among those with ISH may be attributed to both an elevated SBP and a decreased DBP. However, an elevated SBP alone with a normal DBP may also increase the risk of adverse cardiovascular events including incident HF.[1] In a propensity-matched cohort of CHS participants in which those with and without ISH were balanced on 64 baseline characteristics including a mean DBP of 71 mm Hg in both groups, ISH was independently associated with a significant 26% higher risk of developing new-onset HF.[1] The mean SBP of participants with SDH in our study was 12 mm Hg higher than that in the SDH group (Table 1). Yet, the risk of incident HF was rather similar in both groups, suggesting that either an elevated DBP may have attenuated the risk in the SDH group, or a decreased DBP may have increased the risk in the ISH group.

The mean DBP in the ISH group in our study was 19 mm Hg lower than that in the SDH group. Little is known about the association of an isolated elevation of DBP with incident HF in older adults. We have demonstrated that isolated diastolic hypertension, defined as DBP ≥90 mm Hg and SBP <140 mm Hg, a rare form of hypertension in older adults, may be associated with a higher risk of incident HF.[12] In contrast, a low DBP has been shown to be a risk factor for incident HF in this population.[8] In a propensity-matched cohort of CHS participants in which those with and without isolated diastolic hypotension (DBP <60 mm Hg) were balanced on 58 baseline characteristics including a mean SBP of 130 and 131 mm Hg (among those with and without diastolic hypotension, respectively), DBP <60 mm Hg was independently associated with a significant 33% higher risk of developing new-onset HF.[8] Although participants with DBP <60 mm Hg were excluded from our analysis, the mean DBP in the ISH group was 19 mm Hg lower than that in the SDH group (Table 1). Furthermore, with a mean DBP (±SD) of 76 (±8) mm Hg, about a third of those with ISH in our study had DBP <68 mm Hg. Thus, a low DBP in the ISH group may have accentuated the risk of HF in that group despite a lower mean SBP in that group, thus explaining similar risk of HF in both ISH and SDH.

Because of the age-related atherosclerotic changes in large capacitance vessels, hypertension in older adults is more likely to be ISH. However, it is also possible that some patients with

treated SDH in whom SBP may have responded more favorably than DBP would be misclassified as ISH. Findings from randomized controlled trials of hypertension suggest that SBP may be more responsive to antihypertensive therapy than DBP.[13,14] This non-random misclassification may have attenuated a differential association that the two types of hypertension may have with incident HF.[15] In contrast, ISH is unlikely to be misclassified as SDH because by definition patients with ISH would have a normal or low DBP before treatment is initiated and DBP would unlikely be elevated after initiation of therapy. Therefore, patients in the SDH group in our study represent those with true SDH as opposed to being diluted by those with misclassified ISH. Thus, both higher SBP and DBP may have contributed to the higher risk of HF in the SDH group,[12] and a low to low-normal DBP may have been accentuated the risk of HF in the ISH group.[8] It is possible that without the confounding association of low DBP with incident HF in ISH, the true risk of HF in ISH would be lower than that in SDH.

There are limited data in the literature on association of SDH with cardiovascular outcomes. In one study, ISH was associated with a higher prevalence of left ventricular hypertrophy than SDH.[16] This is in contrast to our study where there was no significant difference in the prevalence of left ventricular hypertrophy between the two hypertension groups. This is likely due to the fact that in the prior study ISH was defined as SBP ≥140 mm Hg and DBP <90 mm Hg and these patients had a mean SBP that was 11 mm Hg higher than in the SDH group.[16] This study did not present data on associations with outcomes. In another study, relatively younger Japanese rural patients (mean age, 65 years) with SDH (home SBP ≥137 and DBP ≥84 mm Hg) had higher risk of cardiovascular morbidity and mortality.[17] To the best of our knowledge, this is the first report of comparative associations of SDH and ISH with adverse cardiovascular outcomes in older Americans.

The clinical benefit of BP control in older adults with ISH is well established. In the SHEP trial, in patients (mean age, 72 years) with ISH (SBP ≥160 and DBP <90 mm Hg; mean SBP 171 and DBP 77 mm Hg), antihypertensive drugs significantly reduced the risk of incident HF and stroke, but not of cardiovascular death.[13] In the HYVET trial, in patients (mean age, 84 years) with hypertension (SBP ≥160 mm Hg; mean SBP 173 and DBP 91 mm Hg), antihypertensive drugs significantly reduced the risk of stroke and cardiovascular death, but not of HF.[14] Because two thirds of HYVET participants had SDH (versus 12% among community-dwelling older CHS participants in the current analysis), these findings suggest clinical benefit of BP control in older adults with SDH. However, because of the substantial overlap in cardiovascular risks between ISH and SDH observed in the current study, evidence from trials in ISH and SDH may be generalizable to SDH and ISH, respectively, and vice versa. Findings from the SPRINT older subgroup trial that enrolled older patients (mean age, 80 years) with relatively milder hypertension (SBP ≥130 mm Hg; mean SBP 142 and DBP 72 mm Hg) also support clinical benefit of BP control in older adults with hypertension, regardless of either or both SBP and DBP are elevated.[18]

Several limitations of our study need to be acknowledged. As in any observational epidemiological study, bias due to residual confounding is possible. It is also possible that the small number of patients with SDH may result in chance associations. However, consistent associations across outcomes and lack of association with non-cardiovascular

mortality point to biological plausibility. As discussed above, regression dilution and potential underestimation of true associations is possible.[19]

5. Conclusions

Among community-dwelling older adults, both SDH and ISH have similar independent associations with incident HF, cardiovascular mortality and other incident cardiovascular events. These findings highlight the importance of treatment of hypertension in older adults in order to reduce the burden of cardiovascular morbidity and mortality.

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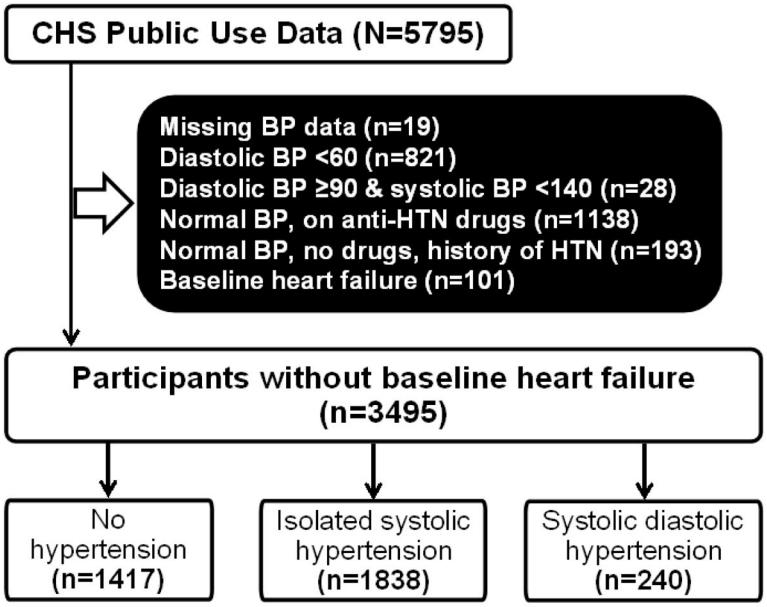

Figure 1.

Flow chart displaying assembly of study cohort based on the public-use copy of the Cardiovascular Health Study (CHS) data (BP=blood pressure; HTN=hypertension)

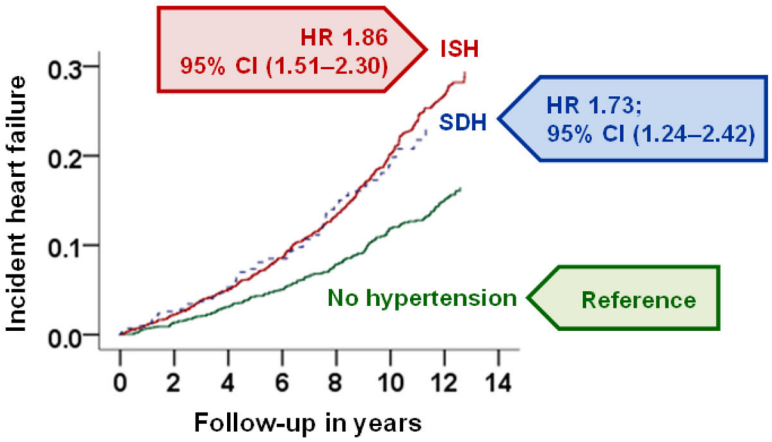

Figure 2.

Multivariable-adjusted plots for incident heart failure by isolated systolic hypertension (ISH), systolic-diastolic hypertension (SDH), and no hypertension

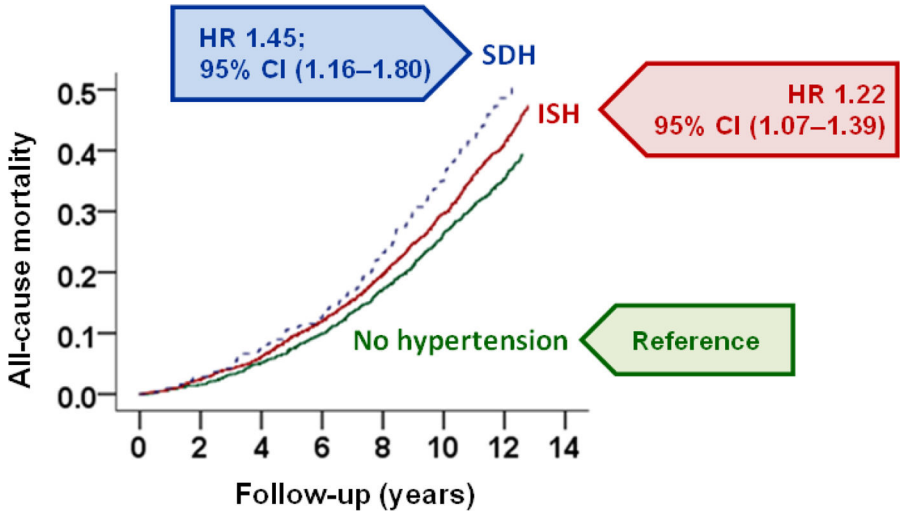

Figure 3.

Multivariable-adjusted plots for all-cause mortality by isolated systolic hypertension (ISH), systolic-diastolic hypertension (SDH), and no hypertension

Table 1

Baseline characteristics by isolated systolic hypertension, systolic-diastolic hypertension and no hypertension among 3495 community-dwelling older adults in the CHS

Mean (±SD) or n (%)	Normal blood pressure (n=1417)	Isolated systolic hypertension (n=1838)	Systolic-diastolic hypertension (n=240)	P value
Age, years	72 (±5)	74 (±6)	73 (±6)	<0.001
Female	785 (55%)	1117 (61%)	105 (44%)	<0.001
African American	143 (10%)	326 (18%)	79 (33%)	<0.001
Education higher than high school	687 (49%)	765 (42%)	95 (40%)	0.001
Income >25K	597 (42%)	601 (33%)	85 (35%)	<0.001
Alcohol, drinks per week	2.6 (±6)	2.6 (±7)	2.9 (±8)	0.814
Smoke, pack-years	17 (±26)	16 (±27)	17 (±26)	0.302
Body mass index, kg/m^2	26.0 (±3.8)	26.9 (±4.1)	27.2 (±4)	0.001
Systolic blood pressure, mm Hg	121 (±12)	156 (±14)	168 (±18)	<0.001
Diastolic blood pressure, mm Hg	69 (±7)	76 (±8)	95 (±5)	<0.001
Pulse pressure, mm Hg	52 (±10)	80 (±14)	73 (±18)	<0.001
Medical problems				
Coronary heart diseases	99 (7%)	314 (17%)	29 (12%)	0.001
Acute myocardial infarction	41 (3%)	139 (8%)	12 (5%)	0.001
Angina pectoris	81 (6%)	267 (15%)	24 (10%)	0.001
Hypertension	0 (0%)	1838 (100%)	240 (100%)	<0.001
Antihypertensive drug use	0 (0%)	971 (53%)	142 (59%)	<0.001
Antihypertensive drugs, number	0 (±0)	1.5 (±0.7)	1.5 (±0.7)	0.866 *
Diabetes mellitus	114 (8%)	332 (18%)	43 (18%)	<0.001
Stroke	26 (2%)	90 (5%)	13 (5%)	0.001
Transient ischemic attack	15 (1%)	59 (3%)	7 (3%)	<0.001
Atrial fibrillation	27 (2%)	35 (2%)	9 (4%)	0.148
Chronic kidney disease	183 (13%)	421 (23%)	53 (22%)	<0.001
Chronic obstructive pulmonary disease	166 (12%)	238 (13%)	26 (11%)	0.439
Arthritis	643 (45%)	981 (53%)	122 (51%)	0.001
Cancer	207 (15%)	252 (14%)	33 (14%)	0.757
LVH by electrocardiogram	18 (1%)	128 (7%)	23 (10%)	<0.001
LV systolic dysfunction by echocardiogram	68 (5%)	131 (7%)	26 (11%)	0.001
Geriatric problems				
Mini mental state examination score	27.9 (±2.3)	27.3 (±2.8)	26.9 (±3.3)	<0.001
Depression score	4.3 (±4.3)	4.6 (±4.4)	4.8 (±4.6)	0.057
Able to walk half a mile	1270 (90%)	1474 (80%)	203 (85%)	<0.001
IADL impairment score	0.24 (±0.58)	0.39 (±0.80)	0.29 (±0.63)	<0.001
Laboratory measures				
Serum glucose, mg/dL	103 (±24)	113 (±35)	114 (±34)	<0.001
Serum creatinine, mg/dL	0.90 (±0.24)	0.96 (±0.37)	1.0 (±0.35)	0.001
Serum potassium, mEq/L	4.3 (±0.29)	4.1 (±0.39)	4.1 (±0.38)	<0.001

Mean (±SD) or n (%)	Normal blood pressure (n=1417)	Isolated systolic hypertension (n=1838)	Systolic-diastolic hypertension (n=240)	P value
Serum cholesterol, mg/dL	211 (±38)	214 (±39)	210 (±39)	0.034
Serum triglyceride, mg/dL	128.6 (±63.3)	143.4 (±82.8)	135.3 (±75.6)	<0.001
Serum albumin, g/dL	4.0 (±0.3)	4.0 (±0.3)	4.0 (±0.3)	0.015
Serum uric acid, mg/dL	5.3 (±1.3)	5.6 (±1.5)	5.7 (±1.5)	<0.001
Fibrinogen, mg/dL	313 (±62)	324 (±66)	331 (±69)	<0.001
Serum coagulation factor-VII	121 (±27)	120 (±29)	123 (±29)	<0.001
Serum interleukin-6, pg/mL	2.0 (±1.7)	2.3 (±1.9)	2.4 (±1.9)	<0.001
Serum insulin, μIU/mL	14.0 (±17.0)	17.5 (±27.9)	16.8 (±26.1)	0.001
Serum C-reactive protein, mg/dL	3.8 (±6.7)	4.8 (±7.8)	5.4 (±10.3)	0.001
Hemoglobin, g/dL	14.1 (±1.29)	14.0 (±1.29)	14.3 (±1.48)	0.001
Platelet count, 10^3/μL	249 (±68)	253 (±77)	254 (±74)	0.275

* p value based on comparison between 971 and 141 patients with isolated systolic hypertension and systolic-diastolic hypertension who received antihypertensive drugs

Table 2

Association of isolated systolic hypertension and systolic-diastolic hypertension with incident heart failure (HR=hazard ratio; CI=confidence interval)

	events (%)	Unadjusted HR (95% CI)	Age-sex-race adjusted HR (95% CI)	Multivariable-adjusted HR* (95% CI)
Normal blood pressure (n=1417)	159 (11%)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Isolated systolic hypertension (n=1838)	466 (25%)	2.75 (2.30–3.30); p<0.001	2.40 (1.99–2.88); p<0.001	1.86 (1.51–2.30); p<0.001
Systolic-diastolic hypertension (n=240)	53 (22%)	2.48 (1.82–3.39); p<0.001	2.19 (1.60–3.00); p<0.001	1.73 (1.24–2.42); p=0.001

*Adjusted with age, sex, race, income, alcohol, smoking, body mass index, general health, kilocalories spent in physical activities, ability to talk half a mile, prior acute myocardial infarction, diabetes, chronic kidney disease, stroke, peripheral arterial disease, atrial fibrillation, left ventricular hypertrophy, left ventricular systolic dysfunction, serum glucose, creatinine, uric acid, fibrinogen, interleukin-6, insulin and C-reactive protein, hemoglobin, and use of anti-hypertensive drugs

Table 3

Association of isolated systolic hypertension and systolic-diastolic hypertension with mortality (HR=hazard ratio; CI=confidence interval)

Hypertension	events (%))	Unadjusted HR (95% CI)	Age-sex-race adjusted HR (95% CI)	Multivariable-adjusted HR* (95% CI)
All–cause mortality				
Normal blood pressure (n=1417)	479 (34 %)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Isolated systolic hypertension (n=1838)	899 (49 %)	1.71 (1.53–1.91); p<0.001	1.41 (1.25–1.57); p<0.001	1.22 (1.07–1.39); p =0.004
Systolic-diastolic hypertension (n=240)	121 (50%)	1.86(1.52–2.27); p<0.001	1.58 (1.29–1.93); p<0.001	1.45 (1.16–1.80); p=0.001
Cardiovascular mortality				
Normal blood pressure (n=1417)	127 (9%)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Isolated systolic hypertension (n=1838)	405 (22%)	2.89 (2.36–3.53); p<0.001	2.38 (1.94–2.91); p<0.001	1.88 (1.49–2.37); p<0.001
Systolic-diastolic hypertension (n=240)	57 (24%)	3.27(2.39–4.48); p<0.001	2.79 (2.03–3.83); p<0.001	2.30 (1.64–3.24); p<0.001
Non-cardiovascular mortality				
Normal blood pressure (n=1417)	350 (25%)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Isolated systolic hypertension (n=1838)	490 (27%)	1.28 (1.11–1.47); p<0.001	1.05 (0.91–1.20); p=0.501	0.97 (0.82–1.15); p=0.734
Systolic-diastolic hypertension (n=240)	64 (27%)	1.35(1.03–1.76); p=0.027	1.14 (0.87–1.49); p=0.325	1.13 (0.84–1.50); p=0.418

*Adjusted with age, sex, race, income, alcohol, smoking, body mass index, general health, kilocalories spent in physical activities, ability to talk half a mile, prior acute myocardial infarction, diabetes, chronic kidney disease, stroke, peripheral arterial disease, atrial fibrillation, left ventricular hypertrophy, left ventricular systolic dysfunction, serum glucose, creatinine, uric acid, fibrinogen, interleukin-6, insulin and C-reactive protein, hemoglobin, and use of anti-hypertensive drugs

Table 4

Association of isolated systolic hypertension and systolic-diastolic hypertension with other incident cardiovascular events (HR=hazard ratio; CI=confidence interval)

	events (%))	Unadjusted HR (95% CI)	Age-sex-race adjusted HR (95% CI)	Multivariable-adjusted HR† (95% CI)
Acute myocardial infarction* (n=392)				
Normal blood pressure (n=1428)	115 (8%)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Isolated systolic hypertension (n=1918)	237 (12%)	1.88 (1.51–2.36); p<0.001	1.82 (1.45–2.29); p<0.001	1.65 (1.27–2.14); p<0.001
Systolic-diastolic hypertension (n=250)	40 (16%)	2.56 (1.78–3.66); p<0.001	2.35 (1.60–3.31); p<0.001	2.09 (1.41–3.10); p<0.001
Angina pectoris* (n=610)				
Normal blood pressure (n=1345)	188 (14%)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Isolated systolic hypertension (n=1609)	361 (22%)	1.89 (1.58–2.25); p<0.001	1.88 (1.57–2.25); p<0.001	1.65 (1.35–2.03); p<0.001
Systolic-diastolic hypertension (n=219)	61 (28%)	2.52 (1.89–3.37); p<0.001	2.18 (1.72–3.09); p<0.001	2.01 (1.46–2.76); p<0.001
Stroke* (n=469)				
Normal blood pressure (n=1402)	111 (8%)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Isolated systolic hypertension (n=1816)	333 (18%)	2.75 (2.22–3.41); p<0.001	2.40 (1.92–2.98); p<0.001	2.06 (1.60–2.64); p<0.001
Systolic-diastolic hypertension (n=235)	45 (19%)	2.91 (2.06–4.12); p<0.001	2.77 (1.95–3.93); p<0.001	2.30 (1.58–3.35); p<0.001
Transient ischemic attack* (n=126)				
Normal blood pressure (n=1412)	34 (2%)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Isolated systolic hypertension (n=1850)	85 (5%)	2.17 (1.45–3.23); p<0.001	2.12 (1.41–3.19); p<0.001	1.72 (1.07–2.78); p=0.025
Systolic-diastolic hypertension (n=243)	7 (3%)	1.38 (0.61–3.11); p=0.417	1.39 (0.61–3.15); p=0.432	1.07 (0.45–2.55); P=0.881
Peripheral arterial disease* (n=83)				
Normal blood pressure (n=1376)	23 (2%)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Isolated systolic hypertension (n=1645)	55 (3%)	2.23 (1.37–3.63); p=0.001	1.97 (1.20–3.24); p=0.007	0.95 (0.48–1.84); p=0.872
Systolic-diastolic hypertension (n=217)	5 (2%)	1.57 (0.59–4.14); p=0.359	1.30 (0.49–3.47); p=0.589	0.65 (0.22–1.95); p=0.450
Coronary artery bypass graft surgery* (n=177)				
Normal blood pressure (n=1394)	58 (4%)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Isolated systolic hypertension (n=1818)	102 (6%)	1.57 (1.14–2.17); p=0.006	2.01 (1.44–2.77); p<0.001	1.80 (1.24–2.62); p=0.002
Systolic-diastolic hypertension (n=244)	17 (7%)	2.05 (1.19–3.52); p=0.009	2.02 (1.17–3.48); p=0.011	1.63 (0.90–2.97); p=105

*Exclude prevalent disease cases

†Adjusted with age, sex, race, income, alcohol, smoking, body mass index, general health, kilocalories spent in physical activities, ability to talk half a mile, prior acute myocardial infarction, diabetes, chronic kidney disease, stroke, peripheral arterial disease, atrial fibrillation, left ventricular hypertrophy, left ventricular systolic dysfunction, serum glucose, creatinine, uric acid, fibrinogen, interleukin-6, insulin and C-reactive protein, hemoglobin, and use of anti-hypertensive drugs