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Uncontrolled Hypertension and Increased Risk for Incident Heart Failure in Older Adults with Hypertension: Findings from a Propensity-Matched Prospective Population Study

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Abstract

Background—Hypertension is a risk factor for incident heart failure (HF). However, the effect of uncontrolled blood pressure (BP) on incident HF in older adults with hypertension has not been prospectively examined in propensity-matched studies.

Methods—Of the 5795 Cardiovascular Health Study participants, ≥65 years, 2562 with self-reported physician-diagnosed hypertension had no baseline HF. Of these, 1391 had uncontrolled hypertension, defined as systolic BP (SBP) ≥140 (n=1373) or diastolic BP ≥90 mm Hg (n=18). Propensity scores for uncontrolled hypertension, calculated for each participant, were used to assemble a cohort of 1021 pairs of participants with controlled and uncontrolled hypertension who were balanced on 31 baseline characteristics.

Results—Centrally adjudicated incident HF developed in 23% and 26% of participants with controlled and uncontrolled hypertension respectively during 13 years of follow-up (matched hazard ratio {HR} when uncontrolled hypertension was compared with controlled hypertension, 1.39; 95% confidence interval {CI}, 1.12–1.73; P=0.003). HR's (95% CI's) for incident HF for those with (n=503) and without (n=1539) chronic kidney disease (CKD) were 1.73 (95% CI, 1.26–2.38; P=0.001) and 1.08 (95% CI, 0.87–1.34; P=0.486) respectively (P for interaction, 0.012). Compared with participants with controlled hypertension, HR's for incident HF associated with

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SBP 140–159 and ≥ 160 mm Hg were 1.06 (95% CI, 0.86–1.31; $P=0.572$) and 1.58 (95% CI, 1.27–1.96; $P<0.0001$) respectively.

Conclusions—In community-dwelling older adults with hypertension, those with uncontrolled (versus controlled) BP has increased risk of new-onset HF, which is more pronounced in those with SBP ≥ 160 mm Hg and with CKD.

Keywords

Hypertension; uncontrolled blood pressure; incident heart failure

Hypertension is common in older adults and is a known risk factor for incident heart failure (HF).^{1–4} Hypertension is often poorly controlled and the risk of cardiovascular morbidity and mortality may be higher in hypertensive patients with uncontrolled hypertension.^{5, 6} However, little is known about the impact of uncontrolled hypertension on incident HF among community-dwelling older adults with hypertension. In the current analysis, we examined the effect of uncontrolled hypertension on incident HF in a propensity-matched cohort of Cardiovascular Health Study (CHS) participants with a history of hypertension and without HF at baseline.

METHODS

Study design and participants

We obtained public-use copies of the CHS from the National Heart, Lung, and Blood Institute, which funded the study. The CHS is an ongoing epidemiologic study of cardiovascular disease in community-dwelling older adults. The design of the CHS has been described in detail elsewhere.⁷ Briefly, 5888 community-dwelling older adults ≥ 65 years were recruited from four US counties from four states in two phases: an original cohort of 5201 mostly white participants (1989–1990) was later supplemented with a cohort of 687 African Americans (1992–1993).⁸ The current analysis is based on both cohorts and included 5795 participants as 93 participants declined to be included in the public-use copy of the database.^{4, 9–11}

Assembling a cohort with hypertension without baseline heart failure

Of the 5795 participants, 2730 (47%) had a history of hypertension at baseline. Data on a history of hypertension was obtained by self-reports of physician-diagnosed hypertension. After excluding 168 participants with prevalent HF at baseline, the final sample size for the current analysis consisted of 2562 participants. Baseline HF was adjudicated by a central CHS Events Committee.^{12, 13}

Baseline blood pressure and other measurements

Baseline seated blood pressure (BP) was measured using a random-zero sphygmomanometer, model 7076 (Hawksley and Sons Limited).¹ The average of two measurements of systolic BP (SBP) and diastolic BP (DBP), corrected for zero values, was used. We defined uncontrolled hypertension as SBP ≥ 140 mm Hg ($n=1373$) or DBP ≥ 90 mm Hg ($n=18$).^{2, 6} Of the 2562 CHS participants, 1391 (54%) had uncontrolled hypertension, nearly 99% of whom had uncontrolled SBP. Most patients received only one anti-hypertensive medication (angiotensin converting enzyme inhibitors, diuretics, calcium channel blockers, beta blockers, or vasodilators) and $<10\%$ were receiving 3 or more anti-hypertensive drugs. Data on socio-demographic, clinical, subclinical, and laboratory variables were collected at baseline.⁷ Chronic kidney disease (CKD) was defined as estimated glomerular filtration rate <60 ml/min/1.73 meter square.^{14, 15}

Incident heart failure and other outcomes

The primary outcome for this study was incident HF during a total of 13 years of follow-up (mean, 9.7 years). Because CHS was primarily a study of cardiovascular disease, it used a rigorous process of adjudication of all cardiovascular outcomes including incident HF. The adjudication of incident HF in CHS has been well-described in the literature and shown to be more stringent than the Framingham criteria for HF.^{8, 12, 13, 16, 17} Briefly, data on self-reports of physician-diagnosed HF were collected during semiannual visits, which was then adjudicated by the CHS Events Committee. A diagnosis of HF was confirmed by examination and retrospective surveillance of participants' medical records for a constellation of symptoms, signs, and other supporting evidence of HF including the use of common HF medications.^{8, 12} Secondary outcomes for the current analysis were all-cause mortality, acute myocardial infarction, angina, stroke, and peripheral artery disease.

Assembly of a balanced cohort with controlled and uncontrolled hypertension

We used propensity score-matching to assemble a cohort in which patients with controlled and uncontrolled hypertension would be balanced on all measured baseline characteristics (Table 1 and Figure 1). The propensity score for uncontrolled hypertension for a patient would be that patient's conditional probability of having an uncontrolled hypertension given his/her measured baseline characteristics.^{18, 19} We began by estimating propensity scores for uncontrolled hypertension for each of the 2562 patients using a non-parsimonious multivariable logistic regression model. In the model uncontrolled hypertension was the dependent variable and the 31 baseline characteristics (Figure 1) were used as covariates.

Because propensity score models are sample-specific adjusters and are not intended for out-of-sample prediction or estimation of coefficients, traditional measures of fitness and discrimination are less relevant and instead their effectiveness is measured by their ability to reduce bias after matching.^{20, 21} Using a greedy matching protocol, described in detail elsewhere, we were able to match 1021 patients with uncontrolled hypertension with 1021 participants with controlled hypertension who had similar propensity scores.^{22–26} We assessed pre- and post-match balance by estimating absolute standardized differences for measured baseline covariates between patients with controlled and uncontrolled hypertension and displayed the results as Love plots (Figure 1).^{22, 26–28} An absolute standardized difference of 0% for a covariate indicates that there is no between-group imbalance on that covariate and values <10% indicate inconsequential imbalance.^{21, 27, 28}

Statistical analysis

For descriptive analyses, we used Pearson Chi square and Wilcoxon rank-sum tests for the pre-match data, and McNemar's test and paired sample t-test for post-match comparisons, as appropriate. Kaplan-Meier and matched Cox regression models were used to estimate the association between uncontrolled hypertension and outcomes. Proportional hazards assumptions were checked using log-minus-log scale survival plots. Select subgroup analyses were conducted to test for heterogeneity of the association between uncontrolled BP and incident HF. In order to assess the effect of loss of participants during matching, we repeated our analysis in all 2562 pre-match participants using three different Cox regression approaches: (1) unadjusted, (2) multivariable-adjusted, using all covariates used in the propensity score model, and (3) propensity score-adjusted. To determine a dose-response relationship, we compared the association between SBP 140–159 mm Hg and ≥ 160 mm Hg on outcomes relative to SBP <140 mm Hg. All statistical tests were 2-sided, and tests with p-values <0.05 were considered significant. SPSS for Windows version 15 was used for all data analysis.²⁹

Sensitivity analysis

Although our matched cohort was well balanced on measured covariates, to determine whether an imbalanced unmeasured covariate may have confounded our findings, we conducted a formal sensitivity analysis to quantify the degree of a hidden bias that would be required to be present to invalidate our main conclusions.³⁰

RESULTS

Baseline characteristics

Overall, matched participants had a mean ($\pm$ SD) age of 73 ($\pm$ 5) years, 60% were women and 21% were African Americans. Before matching, those with uncontrolled hypertension were older with a higher prevalence of left ventricular hypertrophy (LVH) and a lower prevalence of coronary artery disease (CAD; Table 1). Before matching, 19% and 22% of patients with controlled and uncontrolled hypertension were receiving no anti-hypertensive medications ($P=0.036$; Table 1). These and other imbalances in baseline characteristics between patients with and without uncontrolled hypertension were balanced after matching (Table 1 and Figure 1). Post-match absolute standardized differences of $<10\%$ for all measured covariates suggest substantial covariate balance across the groups (Figure 1).

Association of uncontrolled hypertension with incident heart failure

Overall, 497 matched participants (24%) developed incident HF during 18351 person-years of follow-up (Table 2). New-onset HF developed in 23% and 26% of participants with controlled and uncontrolled hypertension respectively (matched hazard ratio {HR} when uncontrolled hypertension was compared with controlled hypertension, 1.39; 95% confidence interval {CI}, 1.12–1.73; $P=0.003$; Table 2 and Figure 2). This association was homogenous across various subgroups of CHS participants except for CKD (Figure 3). In the absence of hidden bias, a sign-score test for matched data with censoring provides strong evidence ($P=0.003$) that those with uncontrolled hypertension clearly developed more new-onset HF than those with controlled hypertension (Table 2). A hidden covariate that is a near-perfect predictor of incident HF would need to increase the odds of uncontrolled hypertension by 12% to explain away this association. Unadjusted and risk-adjusted associations between uncontrolled hypertension and incident HF before matching are displayed in Table 2.

Association of uncontrolled hypertension with other outcomes

A total of 936 (46%) matched participants died from all causes during 18351 person-years of follow-up. All-cause mortality occurred in 44% and 48% of participants with controlled and uncontrolled hypertension respectively (matched HR associated with uncontrolled hypertension, 1.21; 95% CI, 1.04–1.41; $P=0.014$; Table 3). Associations of uncontrolled hypertension with other outcomes are displayed in Table 3.

Dose-response association between uncontrolled hypertension and outcomes

Incident HF occurred in 22%, 23% and 31% of matched patients with SBP <140 mm Hg, 140–159 mm Hg and ≥ 160 mm Hg respectively. Compared with SBP <140 mm Hg, HRs for incident HF associated with SBP 140–159 mm Hg and ≥ 160 mm Hg were 1.06 (95% CI, 0.86–1.31; $P=0.572$) and 1.58 (95% CI, 1.27–1.96; $P<0.0001$) respectively (Table 4). When we compared the rate of incidence HF among those with SBP 120–139 (compared with systolic BP <120 and 120–139 mm Hg (data not shown). The association between uncontrolled SBP and other outcomes are displayed in Table 4.

Effect modification by the presence of chronic kidney disease

Uncontrolled hypertension-associated increase in the risk of incident HF was only observed among those with baseline CKD (HR, 1.73; 95% CI, 1.26–2.38; $P=0.001$) but not among those without CKD (HR, 1.08; 95% CI, 0.87–1.34; $P=0.486$; P for interaction, 0.012; Figure 3). No such interaction was observed by the presence or absence of diabetes (Figure 3). Among matched patients without CKD, incident HF occurred in 21%, 20% and 27% of those with SBP <140, 140–159 and ≥ 160 mm Hg respectively (Table 5). Respective rates for those with CKD were 26%, 33% and 42%. HR's (95% CI's) for incident HF associated with SBP 140–159 mm Hg and ≥ 160 mm Hg (relative to SBP <140 mm Hg) were 1.44 (0.99–2.09; $P=0.054$) and 2.33 (1.59–3.41; $P<0.0001$) respectively among those with CKD (Table 5). There was no such dose-response in the association between uncontrolled hypertension and incident HF among those with diabetes.

DISCUSSION

The findings of the current analysis demonstrate that the presence of uncontrolled hypertension was highly prevalent (54%) among community-dwelling older adults with a history of hypertension and was associated with many baseline characteristics including older age, LVH and underutilization of anti-hypertensive medications. We also demonstrate that uncontrolled hypertension was associated with increased risk of incident HF and that the risk was significant only for those with SBP ≥ 160 mm Hg except for those with CKD, in whom the risk seemed to increase at SBP ≥ 140 mm Hg. Uncontrolled hypertension was also associated with increased risk of other cardiovascular morbidity and mortality. These findings highlight the importance of hypertension control, in particular the control of SBP, in reducing the incidence of HF and other adverse outcomes in older adults with hypertension. This is important as hypertension has the highest attributable risk for incident HF, and can often be easily controlled.^{2, 8, 31}

There are three potential explanations for the observed association between uncontrolled hypertension and incident HF: (1) residual confounding by measured baseline characteristics, (2) confounding by an unmeasured baseline characteristic, or (3) an intrinsic effect of uncontrolled hypertension. We note that before matching, many of the known risk factors for incident HF such as diabetes mellitus and chronic kidney disease were well-balanced between patients with controlled and uncontrolled hypertension. Interestingly, the prevalence of other risk factors such as CAD, smoking and mean serum uric acid levels were even lower in those with uncontrolled hypertension. On the other hand, the prevalence of some of the risk factors such as older age and LVH were higher among patients with uncontrolled hypertension. It is possible that the bivariate association between uncontrolled hypertension and incident HF may in part be explained by the older age and a higher prevalence of LVH among those with uncontrolled hypertension. However, our matched patients were balanced on these and other measured baseline covariates. Therefore, uncontrolled hypertension-associated increased incidence of HF observed in our study may not be explained by imbalances in any of the measured baseline characteristics.

Findings from our sensitivity analysis suggest that the association between uncontrolled hypertension and incident HF observed in our study was rather robust and insensitive to a potential unmeasured confounder. Further, any potential unmeasured confounder must be a near-perfect predictor of incident HF and must not be strongly correlated with any of the many measured covariates used in our study. Because we accounted for most known major risk factors for HF and because HF risk factors are generally correlated with each other, it is unlikely that an unmeasured covariate can confound the association observed in our study. For example, we did not have data on the length of hypertension or the history of

hypertension control. However, LVH is a marker of duration and control of hypertension,^{31, 32} and our matched patients were balanced on baseline LVH.

LVH and CAD are widely believed to represent early pathogenetic pathways to left ventricular systolic and diastolic dysfunction leading to incident HF in patients with hypertension.³³ The baseline prevalence of CAD and AMI was lower in patients with uncontrolled hypertension in our study suggesting that LVH may have played a greater role in the pathogenesis of HF in those with uncontrolled hypertension. However, the prevalence of LVH was balanced in our matched cohort. It is possible that more matched patients with uncontrolled hypertension developed LVH during follow-up.^{31, 32} Because the prevalence of LVH was low (n=84) in our study, the attributable risk of LVH is likely also to be low. A retrospectively analysis of our data demonstrates that 41% of the 84 matched patients with LVH in our study developed incident HF, who represented only 7% of the 497 cases of incident HF. This suggests that factors other than LVH must have played roles in the development of HF in these patients. For instance, it is possible that the subjects with uncontrolled hypertension had developed diastolic dysfunction before developing LVH. In nearly 20% of patients with untreated hypertension and without LVH, left ventricular filling may be abnormal.³⁴ Further, uncontrolled hypertension is a risk factor for CKD, which in turn is a strong predictor of incident HF.^{8, 35} Hypertension is also difficult to control in the presence of CKD.³⁶ It is possible that more matched patients with uncontrolled hypertension developed CKD during follow-up thus increasing the risk of HF.

Several studies have demonstrated an association between hypertension and HF.^{8, 31, 33} Our use of propensity-matched design to assemble a balanced cohort distinguishes our study from those prior studies. Further, unlike the current analysis of CHS, in those studies, patients with hypertension were compared with those without hypertension. We have previously demonstrated that CHS participants with isolated systolic hypertension had higher risk of incident HF compared to propensity-matched participants without isolated systolic hypertension.⁴ In contrast, in the current study, all patients had a history of hypertension, which highlights the importance of optimal control of hypertension. A substantial number of patients in our study were either taking no antihypertensive medications or were receiving one or two medications. It is estimated that most patients may require up to two or more antihypertensive medications to adequately control hypertension.²

Nearly half of the 5795 community-dwelling older adults in CHS had hypertension, over half of whom had uncontrolled hypertension, which was associated with 55 additional cases of incident HF per 10,000 person-years of follow-up. Extrapolated to about 18 million patients with hypertension among nearly 40 million persons ≥ 65 years in the US, an estimated 10 million may have uncontrolled hypertension. This may explain nearly 55,000 of the estimated 670,000 cases of HF that are newly diagnosed each year in the US.³⁷ Isolated systolic hypertension is common in older adults and we noted that nearly 99% of patients with uncontrolled hypertension in our study had uncontrolled SBP. The findings of our study highlight the importance of control of hypertension in older adults in general and in those with CKD and diabetes mellitus in particular. Although some studies have suggested benefit from a more aggressive treatment of SBP, others have failed to confirm that.^{32, 38–41}

Currently there is no randomized clinical trial based evidence suggesting that aggressive lowering of SBP to <140 mm Hg may provide additional benefit in terms of reducing cardiovascular morbidity and mortality.^{39, 40, 42} Findings from our subgroup analyses also suggest that uncontrolled hypertension was a strong and significant predictor of incident HF only among those with CKD but not in those without CKD, and that this difference was statistically significant. Further, for those with CKD, SBP 140–159 mm Hg seemed to

increase the risk of HF. This data suggest that in older adults with hypertension who also have CKD, SBP should be maintained <140 mm Hg. For those without CKD, SBP should be maintained <160 mm Hg. However, considering that those with SBP 140–159 mm Hg may be at increased risk of stroke and unstable angina (Table 4) and that many patients with uncontrolled hypertension in our study were receiving no or only one anti-hypertensive medications, optimizing hypertension control to SBP <140 mm Hg with at least two anti-hypertensive medication would be considered standard of care and would be expected to reduce cardiovascular morbidity.

Our study has several limitations. We identified our study cohort based on self-reported physician-diagnosed hypertension which may have underestimated the true prevalence of hypertension. However, data on all baseline cardiovascular diseases in CHS were collected using a similar method. Uncontrolled hypertension was defined using the average of three baseline BP recording, which may be less reliable than 24-hour recording. However, the higher pre-match prevalence of LVH in our study suggests that those with uncontrolled hypertension may have had their BP uncontrolled for a long period of time. It is possible that participants with controlled hypertension at baseline may have developed uncontrolled hypertension during follow-up and those with uncontrolled hypertension at baseline had their BP controlled during follow-up. However, such regression dilution is likely to underestimate the true association and not pose a threat to the validity of our findings.⁴³

In conclusion, uncontrolled hypertension was common and was associated with increased risk of incident HF and other adverse cardiovascular outcomes among community-dwelling older adults with a history of hypertension. Further, the risk was significant only for those with SBP ≥160 mm Hg, except for those with CKD, in whom the risk seems to increase at SBP ≥140 mm Hg. These findings suggest that in community-dwelling older adults with hypertension, SBP must be kept below 160 mm Hg in general, and below 140 mm Hg for those with CKD.

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Figure 1.

Love plots displaying absolute standardized differences for baseline covariates between participants with controlled and uncontrolled (systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mm Hg) hypertension, before and after propensity score matching

Number of patients at risk

Controlled hypertension	1021	968	890	794	696	501	421
Uncontrolled hypertension	1021	958	868	752	638	452	378

Figure 2.

Kaplan-Meier plots for incident heart failure by uncontrolled hypertension (systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mm Hg) in a propensity-matched cohort of Cardiovascular Health Study participants (CI=confidence interval; HR=hazard ratio)

Figure 3. Association of uncontrolled hypertension (systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mm Hg) with incident heart failure in subgroups of propensity-matched patients (CI=confidence interval)

Table 1

Baseline Characteristics by Uncontrolled Hypertension (systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mm Hg) Before and After Propensity Matching

n (%) or mean ($\pm$ SD)	Before matching			After matching		
	Uncontrolled Hypertension		P	Uncontrolled No (n=1021)	Hypertension Yes (n=1021)	P
	No (n=1171)	Yes (n=1391)				
Age, years	72.3 (± 5.0)	74.0 (± 5.7)	<0.0001	72.6 (± 5.2)	72.9 (± 5.2)	0.162
Female	683 (58.3%)	862 (62.0%)	0.060	609 (59.6%)	609 (59.6%)	1.000
Non-white	223 (19.0%)	340 (24.4%)	0.001	209 (20.5%)	209 (20.5%)	1.000
Married	770 (65.8%)	875 (62.9%)	0.134	684 (67.0%)	654 (64.1%)	0.176
Living alone	163 (13.9%)	219 (15.7%)	0.197	142 (13.9%)	161 (15.8%)	0.260
$\geq$ College education	453 (38.7%)	567 (40.8%)	0.285	404 (39.6%)	411 (40.3%)	0.779
$\geq$ \$25000 annual income	410 (35.0%)	447 (32.1%)	0.124	349 (34.2%)	354 (34.7%)	0.853
Smoker (current)	153 (13.1%)	140 (10.1%)	0.017	117 (11.5%)	129 (12.6%)	0.441
Alcohol intake, units/week	2.49 (± 6.94)	2.40 (± 6.52)	0.032	2.35 (± 6.42)	2.55 (± 6.86)	0.508
Coronary artery disease	275 (23.5%)	262 (18.8%)	0.004	211 (20.7%)	203 (19.9%)	0.692
Myocardial infarction	130 (11.1%)	103 (7.4%)	0.001	94 (9.2%)	90 (8.8%)	0.809
Angina pectoris	225 (19.2%)	230 (16.5%)	0.077	181 (17.7%)	172 (16.8%)	0.639
Coronary artery bypass surgery	65 (5.6%)	48 (3.5%)	0.010	42 (4.1%)	43 (4.2%)	1.000
Atrial fibrillation by electrocardiography	22 (1.9%)	36 (2.6%)	0.229	21 (2.1%)	24 (2.4%)	0.766
Left ventricular hypertrophy by electrocardiography	38 (3.2%)	130 (9.3%)	<0.0001	38 (3.7%)	46 (4.5%)	0.291
Left ventricular systolic dysfunction by echocardiogram	107 (9.1%)	114 (8.2%)	0.398	83 (8.1%)	85 (8.3%)	0.937
Stroke	57 (4.9%)	76 (5.5%)	0.498	46 (4.5%)	54 (5.3%)	0.475
Diabetes mellitus	234 (20.0%)	292 (21.0%)	0.529	207 (20.3%)	204 (20.0%)	0.913
Chronic kidney disease *	304 (26.0%)	350 (25.2%)	0.644	246 (24.1%)	257 (25.2%)	0.572
Chronic obstructive pulmonary disease	141 (12.0%)	188 (13.5%)	0.266	127 (12.4%)	126 (12.3%)	1.000
Cancer	164 (14.0%)	195 (14.0%)	0.992	140 (13.7%)	136 (13.3%)	0.848
Arthritis	635 (54.2%)	783 (56.3%)	0.295	567 (55.5%)	564 (55.2%)	0.930
Body mass index, kg/m ²	27.48 (± 4.13)	27.32 (± 4.19)	0.339	27.40 (± 4.07)	27.34 (± 4.12)	0.733
Pulse rate, beats/min	68 (± 11)	68 (± 12)	0.517	68 (± 11)	68 (± 12)	0.990

n (%) or mean (±SD)	Before matching			After matching		
	Uncontrolled Hypertension		P	Hypertension		P
	No (n=1171)	Yes (n=1391)		Uncontrolled No (n=1021)	Yes (n=1021)	
Blocks walked last week	37.7 (±52.6)	33.1 (±50.5)	0.023	37.1 (±52.0)	35.6 (±52.8)	0.497
15-ft walk time, sec	5.8 (±2.7)	6.0 (±2.2)	0.032	5.8 (±1.9)	5.9 (±2.1)	0.282
Serum creatinine, mg/dL	1.01 (±0.55)	0.99 (±0.39)	0.279	1.00 (±0.56)	0.98 (±0.34)	0.607
Serum potassium, mEq/L	4.06 (±0.42)	4.06 (±0.40)	0.730	4.06 (±0.43)	4.06 (±0.40)	0.894
Serum uric acid, mg/dL	6.13 (±1.60)	5.86 (±1.55)	<0.0001	6.00 (±1.53)	5.98 (±1.52)	0.824
Plasma glucose, mg/dL	117 (±45.0)	116 (±37.8)	0.568	116 (±40.9)	116 (±37.4)	0.886
Serum insulin, mcU/mL	18.6 (±20.2)	18.7 (±30.6)	0.952	18.5 (±21.3)	18.1 (±24.9)	0.726
Albumin, g/dL	4.01 (±0.29)	4.01 (±0.29)	0.743	4.01 (±0.29)	4.01 (±0.29)	0.917
C-reactive protein, mg/dL	5.3 (±8.5)	5.3 (±8.4)	0.949	5.3 (±8.3)	5.3 (±8.6)	0.848
Interleukin 6, pg/mL	2.3 (±1.7)	2.4 (±2.1)	0.260	2.3 (±1.8)	2.3 (±1.5)	0.998
Total cholesterol, mg/dL	211 (±39.9)	213 (±39.1)	0.253	213 (±40)	212 (±39)	0.678
Hemoglobin, g/dL	14.1 (±1.45)	14.0 (±1.34)	0.012	14.0 (±1.4)	14.1 (±1.3)	0.668
White blood cell, 10 ³ /μL	6.40 (±1.95)	6.48 (±2.37)	0.333	6.36 (±1.91)	6.52 (±2.56)	0.101
Platelet, 10 ³ /μL	251 (±81.4)	255 (±77.1)	0.174	251 (±78.8)	255 (±78.3)	0.166
Antihypertensive medications	951 (81.2%)	1083 (77.9%)	0.036	820 (80.3%)	791 (77.5%)	0.136
Number of antihypertensive medications						
0	220 (18.8%)	308 (22.1%)	0.066	201 (19.7%)	230 (22.5%)	0.264
1	525 (44.8%)	614 (44.1%)		457 (44.8%)	453 (44.4%)	
2	365 (31.2%)	384 (27.6%)		308 (30.2%)	272 (26.6%)	
≥3	61 (5.2%)	85 (6.1%)		55 (5.4%)	66 (6.5%)	

* Chronic kidney disease was defined as estimated glomerular filtration rate <60 ml/min/1.73 meter square

Table 2

Association of Uncontrolled Hypertension (systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mm Hg) with Incident Heart Failure

	Rate per 10,000 Person-Years (Events/Total Follow-Up Years)		Absolute Rate Difference* (per 10,000 Person-Years)	Matched Hazard ratio (95% confidence interval)	P value
	Uncontrolled Hypertension				
	No	Yes			
Before matching (n=2562)	n=1171	n=1391			
Unadjusted	248 (268/10804)	310 (367/11839)	+62	1.28 (1.09–1.49)	0.003
Multivariable-adjusted	---	---		1.26 (1.07–1.49)	0.006
Propensity-adjusted	---	---		1.21 (1.03–1.42)	0.021
After matching (n=2042)	n=1021	n=1021			
Propensity-matched	244 (230/9417)	299 (267/8934)	+55	1.39 (1.12–1.73)	0.003

* Absolute rate differences were calculated by subtracting the rates of new-onset heart failure in the controlled hypertension group from those in the uncontrolled hypertension group (before values were rounded).

CI = confidence interval; HR = hazard ratio

Table 3

Association of Uncontrolled Hypertension (systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mm Hg) with Other Outcomes

	Events (%)		Matched Hazard ratio (95% confidence interval)	P
	Uncontrolled Hypertension			
	No (n=1021)	Yes (n=1021)		
All-cause mortality	44%	48%	1.21 (1.04–1.41)	0.014
Acute myocardial infarction	11%	12%	1.29 (0.96–1.74)	0.096
Angina pectoris	15%	19%	1.51 (1.18–1.93)	0.001
Stroke	14%	19%	1.51 (1.17–1.95)	0.002
Peripheral artery disease	4%	6%	1.18 (0.77–1.81)	0.448

Table 4

Systolic Blood Pressure (SBP) and Incident Heart failure in a Propensity-Matched Cohort of Older Adults with Hypertension

		SBP <140 mm Hg (n=1034)	SBP 140–159 mm Hg (n=607)	SBP ≥160 mm Hg (n=401)
Incident HF	% events	22%	23%	31%
	HR (95% CI)	1 (Reference)	1.06 (0.86 – 1.31); P=0.572	1.58 (1.27 – 1.96); P<0.0001
All-cause mortality	% events	44%	43%	55%
	HR (95% CI)	1	0.97 (0.83 – 1.13); P=0.682	1.40 (1.19 – 1.64); P<0.0001
Acute myocardial infarction	% events	11%	12%	12%
	HR (95% CI)	1	1.09 (0.82 – 1.50); P=0.497	1.25 (0.89 – 1.75); P=0.206
Angina pectoris	% events	15%	18%	22%
	HR (95% CI)	1	1.23 (0.97 – 1.57); P=0.095	1.59 (1.22 – 2.06); P=0.001
Stroke	% events	14%	17%	21%
	HR (95% CI)	1	1.25 (0.97 – 1.60); P=0.087	1.64 (1.25 – 2.15); P<0.0001
Peripheral artery disease	% events	4%	4%	8%
	HR (95% CI)	1	1.00 (0.62 – 1.63); P=0.993	2.12 (1.35 – 3.33); P=0.001

CI=confidence interval; HR=hazard ratio

Table 5

Systolic Blood Pressure (SBP) and Incident Heart failure in Propensity-Matched Cohort of Older Adults with Hypertension, by the presence or absence of Chronic Kidney Disease (CKD) and Diabetes Mellitus (DM)

		SBP <140 mm Hg (N=1034)	SBP 140 – 159 mm Hg (N=607)	SBP ≥160 mm Hg (N=401)
No CKD	% events	21%	20%	27%
	HR (95% CI)	1	0.94 (0.73 – 1.21); P=0.617	1.33 (1.02 – 1.74); P=0.036
CKD	% events	26%	33%	42%
	HR (95% CI)	1	1.44 (0.99 – 2.09); P=0.054	2.33 (1.59 – 3.41); P<0.0001
No DM	% events	20%	22%	26%
	HR (95% CI)	1	1.07 (0.84 – 1.36); P=0.598	1.41 (1.08 – 1.84); P=0.012
DM	% events	31%	32%	47%
	HR (95% CI)		1.15 (0.76 – 1.73); P=0.520	2.06 (1.40 – 3.04); P<0.0001

CI = confidence interval; HR = hazard ratio