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

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Abstract

Background—Isolated systolic hypertension and isolated diastolic hypotension are common in older adults and associated with a higher risk of incident heart failure (HF). However, little is known about the prevalence and impact of isolated diastolic hypertension in this population.

Methods—In the Cardiovascular Health Study (CHS), of the 5776 community-dwelling older adults ≥65 years who had data on baseline systolic and diastolic blood pressure (SBP and DBP), 28 had isolated diastolic hypertension (DBP ≥90 mm Hg and SBP <140 mm Hg). From the 5748 without isolated diastolic hypertension, we excluded those with SBP ≥120 mm Hg (n=4451), DBP 80–89 mm Hg (n=20), DBP <60 mm Hg (n=425), normal BP taking anti-hypertensive medications (n=311), normal BP taking no anti-hypertensive medications but with history of hypertension (n=38), and baseline HF (n=5). The final cohort of 524 participants included 27 with isolated diastolic hypertension.

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Conflict of Interest Disclosures: None

Results—Patients (n=524) had a mean (\pm SD) age of 71 (\pm 5) years, 58% were women and 9% African American. There were no significant between-group age or sex differences; 37% of those with isolated diastolic hypertension (versus 7% without) were African American. Incident HF occurred in 19% and 7% of participants with and without isolated diastolic hypertension, respectively (multivariable-adjusted hazard ratio {HR}, 4.65; 95% confidence interval {CI}, 1.09–19.90; p=0.038). There was a trend toward higher cardiovascular mortality (HR, 4.59; 95% CI, 0.92–23.88; p=0.063).

Conclusion—Among community-dwelling older adults, isolated diastolic hypertension is rare and is associated with higher risk for incident HF and cardiovascular mortality.

Keywords

Isolated Diastolic Hypertension; Incident Heart Failure; Mortality

1. Introduction

Isolated systolic hypertension, characterized by an elevation of systolic blood pressure (SBP) without an elevation of diastolic BP (DBP), is the most common form of hypertension among older adults and has been shown to be associated with a higher risk of incident adverse cardiovascular events including heart failure (HF).¹ Because isolated systolic hypertension is also associated with the widening of the pulse pressure, these patients often have normal or low DBP. As such, isolated diastolic hypotension, characterized by a decrease in DBP without a decrease in SBP, is also common in older adults and has also been shown to be associated with a similar risk of incident HF as that of isolated systolic hypertension.² In contrast, little is known about the prevalence and effect of isolated diastolic hypertension in older adults. Characterized by an elevation of DBP without an elevation of SBP, isolated diastolic hypertension is relatively common among younger adults and is generally less harmful than systolic hypertension.^{3–5} In the current study, we examined the association of isolated diastolic hypertension with incident HF and other outcomes in community-dwelling older adults in the Cardiovascular Health Study (CHS).

2. Materials and Methods

2.1. Source of data

The CHS is a prospective population-based study of risk factors for cardiovascular disease among older adults, the details of which has been previously described.⁶ Sponsored by the United States National Heart, Lung, and Blood Institute (NHLBI), between 1989 and 1993 the CHS enrolled 5888 community-dwelling adults \geq 65 years of age from 4 states in the United States. The current analysis is based on a public-use limited-access deidentified copy of the CHS data obtained from the NHLBI that included 5795 individuals, of which 5776 had data on baseline SBP and DBP.

2.2. Isolated diastolic hypertension

Isolated diastolic hypertension was defined as DBP \geq 90 mm Hg and SBP <140 mm Hg. Of the 5776 participants, 28 had isolated diastolic hypertension. Data on BP were collected

using a random-zero sphygmomanometer while participants remained seated and the average of two BP values were used.¹ Of the 5748 participants *without* isolated diastolic hypertension, the following participants were excluded: (1) SBP \geq 120 mm Hg (n=4451), (2) DBP 80–89 mm Hg (n=20), (3) DBP $<$ 60 mm Hg (n=425), (4) normal BP taking anti-hypertensive medications (n=311), (5) normal BP taking no anti-hypertensive medications but with history of hypertension (n=38), and (6) baseline HF (n=5). We excluded participants with SBP 120 to 139 mm Hg and DBP 80 to 89 mm Hg from those without isolated diastolic hypertension to assemble an ideal non-exposed group with normal BP.⁷ SBP 120–139 mm Hg has been shown to be associated with higher risk of cardiovascular events.⁸ We also excluded participants with DBP $<$ 60 mm Hg as this has been shown to be associated with a higher risk of incident HF.² We did not exclude participants with SBP 120 to 139 mm Hg from the isolated diastolic hypertension group because the guideline definition of hypertension includes either SBP $>$ 140 or DBP $>$ 90 mm Hg. Furthermore, as would be expected, all of the 27 patients with isolated diastolic hypertension except for 1 had SBP between 120 and 139 mm Hg. Thus, from a total of 5748 participants without isolated diastolic hypertension, we selected 497 who had normal SBP and DBP. Of the 28 participants with isolated diastolic hypertension, 1 had baseline HF, and was also excluded. Thus, the final cohort consisted of 524 participants of which 27 had isolated diastolic hypertension and 497 had normal BP (SBP $<$ 120 mm Hg and DBP 60–79 mm Hg).

2.3. Study outcomes

The primary outcome for the current analysis was incident HF during 13 years of follow-up. HF was centrally adjudicated and the process has been previously described.^{1,2,9–12} Briefly, self-reports of physician-diagnosed HF was adjudicated through the examination of medical records for physician diagnosis, treatment with HF medications, and other supporting evidence. Secondary outcomes included all-cause, cardiovascular and non-cardiovascular mortality, and incident myocardial infarction and stroke.

2.4. Statistical analysis

Descriptive analyses were conducted using Chi-square and student's t-test as appropriate to compare baseline characteristics of patients with and without isolated diastolic hypertension. Multivariable-adjusted Cox regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for outcomes associated with isolated diastolic hypertension. The model was adjusted for age, sex, race, income, smoking, alcohol use, physical activity, prior acute myocardial infarction (AMI), diabetes, left ventricular hypertrophy, SBP, left ventricular systolic dysfunction, serum creatinine and C-reactive protein. Because participants without isolated diastolic hypertension in our analysis had lower SBP (by design they had SBP $<$ 120 mm Hg), to examine the potential effect of confounding by SBP, we repeated the above model without the SBP. Because patients with isolated diastolic hypertension in older adults may represent a subset of treated systolic-diastolic hypertension with a proportionately better response to SBP than to DBP,^{13,14} we compared baseline characteristics of the 27 patients with isolated diastolic hypertension by receipt of antihypertensive therapy. All statistical tests were two-tailed with a p-value $<$ 0.05 considered significant. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp. was used for data analyses.

3. Results

3.1. Baseline characteristics

Patients (n=524) had a mean (\pm SD) age of 71 (\pm 5) years, 58% were women, and 9% were African American. There were 4 times more African American among those with isolated diastolic hypertension (37% versus 8% of those without), but there was no significant between-group age or sex difference (Table 1). Other baseline characteristics of the study participants are presented in Table 1.

3.2. Isolated diastolic hypertension and incident heart failure

During about 13 years of follow-up, incident HF occurred in 19% and 7% of participants with and without isolated diastolic hypertension, respectively (multivariable-adjusted HR, 4.65; 95% CI, 1.09–19.90; $p=0.038$; Table 2). When we removed SBP from multivariable model, adjusted HR (95% CI) for incident HF was 2.86 (0.97–8.44; $p=0.58$).

3.3. Isolated diastolic hypertension and mortality

All-cause mortality occurred in 41% and 29% of participants with and without isolated diastolic hypertension, respectively (multivariable-adjusted HR, 1.54; 95% CI, 0.64–3.67; Table 2). Cardiovascular mortality occurred in 19% and 7% of participants with and without isolated diastolic hypertension, respectively (multivariable-adjusted HR, 4.59; 95% CI, 0.92–22.88; $p=0.063$; Table 2). Isolated diastolic hypertension had no association with non-cardiovascular death (HR, 0.94; 95% CI, 0.30–2.91; $p=0.915$; Table 2).

3.4. Isolated diastolic hypertension and other cardiovascular events

There were 24 cases of incidence AMI among the 509 participants without a history of AMI at baseline and none occurred in the isolated diastolic hypertension group. There were 27 cases of incident stroke among the 519 participants without a history of stroke at baseline and only one occurred in the isolated diastolic hypertension group.

3.5. Isolated diastolic hypertension and receipt of antihypertensive therapy

There was no significant age difference between patients treated (mean, 71 years) versus not treated (mean, 72 years) with antihypertensive drugs. Similarly there were no differences in sex (43% vs 46% women in the treated and untreated groups, respectively) and race (36% vs 39% African American among those treated and untreated, respectively). There was no difference in mean SBP (133 vs 132 mm Hg for untreated) or DBP (96 vs 94 mm Hg). Of the 5 patients with isolated diastolic hypertension that developed new-onset HF (Table 2), 4 occurred in the group receiving antihypertensive therapy (exact $p=0.326$). Of the 5 cardiovascular deaths in isolated diastolic hypertension group (Table 2), 3 occurred in the group receiving antihypertensive therapy (exact $p=1.00$).

Discussion

Findings from the current analysis demonstrate that the prevalence of isolated diastolic hypertension is low among community-dwelling older adults, and that the presence of isolated diastolic hypertension is associated with a significantly higher risk of incident HF.

Furthermore, isolated diastolic hypertension is also associated with a trend toward a higher risk of cardiovascular death, but has no association with non-cardiovascular death or other cardiovascular events. To the best of our knowledge this is the first study to examine the cardiovascular impact of isolated diastolic hypertension in a major prospective population-based cardiovascular epidemiological study.

An aging-related rise in SBP and drop in DBP due to stiffening of large arteries explains the high prevalence of isolated systolic hypertension and isolated diastolic hypotension in older adults.¹⁵ These age-related vascular changes may also explain the low prevalence of diastolic hypertension in this age group. Although we found no evidence of baseline characteristic differences between treated and untreated patients with isolated diastolic hypertension, it is possible that the treated subset represents partially treated systolic-diastolic hypertension with DBP still in the hypertensive range. A higher mean SBP in the isolated diastolic hypertension group would be expected in part to explain the higher risk of incident HF in that group. Participants without isolated diastolic hypertension in our study had normal SBP (mean, 111 mm Hg; Table 1),⁷ while those with isolated diastolic hypertension included those with pre-systolic-hypertension (SBP 120 to 139 mm Hg),⁷ which has been shown to be associated with higher risk of cardiovascular events.⁸ However, the association of isolated diastolic hypertension with incident HF was not attenuated after adjustment for SBP suggesting that a higher SBP may not explain the observed association. Although we adjusted for prior AMI in our multivariable model, residual confounding is possible.¹⁶ However, the lack of association of isolated diastolic hypertension with incident AMI in our study makes it an unlikely possibility.

There is limited data on prevalence and impact of isolated diastolic hypertension in the literature. In one study, a third of adult men 30–45 years had isolated diastolic hypertension that had no association with mortality.³ In another study, cardiovascular remodeling in older patients with diastolic hypertension was examined, but no association with outcomes was presented.⁴ Another study of young and middle-aged patients reported that isolated diastolic hypertension was associated with a lower risk of incident AMI.⁵ Neither study presented data on association with incident HF. In contrast to these above studies, to the best of our knowledge, these data are the first report of significant associations of isolated diastolic hypertension with adverse cardiovascular outcomes in older adults.

Although the prevalence of isolated diastolic hypertension is low in community-dwelling older adults, the absolute number of older adults with isolated diastolic hypertension nationally and globally would be substantial. For example, based on 2014 census, the number of older adults > 65 years in the United States is 46.2 million and of these over 200,000 would have isolated diastolic hypertension. However, given the low prevalence of isolated diastolic hypertension, it is unlikely that the effect of lower DBP with antihypertensive therapy in this population will be tested in a randomized controlled trial. Thus, considering the beneficial effect of treatment of systolic hypertension,^{13,14,17,18} older adults with isolated diastolic hypertension should be considered for therapy according to the recommendations of hypertension guidelines.

Several limitations of our study need to be acknowledged. Despite multivariable adjustment, bias due to residual confounding is possible. Also, chance association is also possible due to small number of patients with isolated diastolic hypertension. Regression dilution and potential underestimation of true associations is possible.¹⁹

In conclusion, isolated diastolic hypertension is rare among community-dwelling older adults and when present is associated with a higher risk of incident HF and cardiovascular mortality. Future studies need to examine this association in larger and more contemporary populations of older adults.

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**Multivariable-adjusted HR, 4.65;
95% CI, 1.09–19.90; p=0.038**

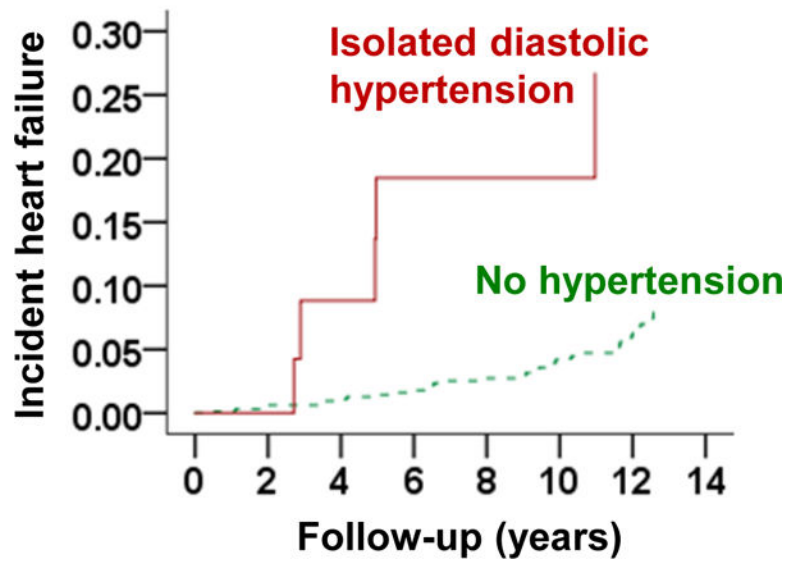


Figure 1. Survival plots for incident heart failure by isolated diastolic hypertension based on multivariable-adjusted Cox regression model (CI=confidence interval)

Table 1

Baseline patient characteristics by isolated diastolic hypertension

| n (%) or mean (\pm SD) | Isolated diastolic hypertension | | P value |
|--------------------------------------|---------------------------------|-------------------|---------|
| | No (n=497) | Yes (n=27) | |
| Age (years) | 71 (\pm 5) | 71 (\pm 6) | 0.927 |
| Female | 293 (59%) | 12 (44%) | 0.137 |
| African American | 38 (8%) | 10 (37%) | <0.001 |
| Annual household income \$25,000 | 227 (46%) | 13 (48%) | 0.802 |
| Smoking (pack-year) | 18 (\pm 27) | 16 (\pm 25) | 0.722 |
| Alcohol (drinks/week) | 2 (\pm 4) | 4 (\pm 7) | 0.077 |
| Instrumental ADL | 0.24 (\pm 0.6) | 0.52 (\pm 0.9) | 0.024 |
| Time to walk 15 feet (seconds) | 5 (\pm 1) | 6 (\pm 2) | 0.034 |
| Body mass index (kg/m ²) | 25 (\pm 4) | 29 (\pm 4) | <0.001 |
| Acute myocardial infarction | 12 (2%) | 3 (11%) | 0.008 |
| Diabetes mellitus | 28 (6%) | 6 (22%) | 0.001 |
| Pulse (beats per minute) | 68 (\pm 10) | 72 (\pm 13) | 0.034 |
| Systolic BP (mm Hg) | 111(\pm 6) | 132 (\pm 6) | <0.001 |
| Diastolic BP (mm Hg) | 67 (\pm 5) | 94 (\pm 5) | <0.001 |
| LV hypertrophy | 2 (0.4%) | 0 (0%) | 0.741 |
| LVEF 55% or higher | 481 (97%) | 22 (82%) | <0.001 |
| Serum creatinine (mg/dl) | 0.9 (\pm 0.2) | 0.9 (\pm 0.2) | 0.587 |
| Serum uric acid (mg/dl) | 5.2 (\pm 1.3) | 6.0 (\pm 1.6) | 0.002 |
| Serum C-reactive protein | 3.3 (\pm 7.0) | 6.5 (\pm 7.3) | 0.017 |
| Serum insulin | 13 (\pm 10) | 19 (\pm 11) | 0.005 |
| ACE inhibitor or ARB use | 0 (0%) | 2 (7%) | <0.001 |
| Beta-blocker use | 0 (0%) | 3 (11%) | <0.001 |
| Thiazide diuretic use | 0 (0%) | 2 (7%) | <0.001 |
| Ca-channel blocker use | 0 (0%) | 6 (22%) | <0.001 |
| Any anti-hypertensive drugs | 0 (0%) | 14 (52%) | <0.001 |

ABBREVIATIONS: ACE=angiotensin converting enzyme; ADL=activities of daily living; ARB= Angiotensin receptor blocker; BMI=body mass index; BP=blood pressure; CABG=coronary artery bypass graft; LVEF=left ventricular ejection fraction

Table 2

Outcomes by isolated diastolic hypertension

| Outcomes | Events (%) | | HR (95% CI) | |
|------------------------------|---------------------------------|------------|----------------------------|----------------------------|
| | Isolated diastolic hypertension | | Age-sex-race-adjusted | Multivariable-adjusted* |
| | No (n=497) | Yes (n=27) | | |
| Incident heart failure | 36 (7%) | 5 (19%) | 3.49 (1.32–9.23); p=0.012 | 4.65 (1.09–19.90); p=0.038 |
| All-cause mortality | 142 (29%) | 11 (41%) | 1.99 (1.06–3.74); p=0.033 | 1.54 (0.64–3.67); p=0.333 |
| Cardiovascular mortality | 33 (7%) | 5 (19%) | 4.72 (1.76–12.61); p=0.002 | 4.59 (0.92–22.88); p=0.063 |
| Non-cardiovascular mortality | 109 (22%) | 5 (19%) | 1.10 (0.44–2.75); p=0.836 | 0.94 (0.30–2.91); p=0.915 |

* Adjusted for age, sex, race, income, smoking, alcohol use, physical activity, prior acute myocardial infarction, diabetes, systolic blood pressure left ventricular systolic dysfunction, serum creatinine and C-reactive protein

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