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Systolic and Diastolic Blood Pressure, Incident Cardiovascular Events and Death in Elderly Persons: The Role of Functional Limitation

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Abstract

Background: Whether limitation in ability to perform activities of daily living (ADL) or gait speed can identify subgroups of elders in whom the association of systolic (SBP) and diastolic (DBP) blood pressure with cardiovascular events and death differs is not well established.

Methods: We evaluated whether ADL and gait speed modify the association of SBP or DBP with incident cardiovascular (CV) events (N= 2,358) and all-cause death (N=3,547) among participants in the 7th visit of the Cardiovascular Health Study. We used multivariable Cox regression adjusting for potential confounders.

Results: Mean age was 78 ± 5 years and 21% reported limitation in ≥1 ADL. There were 778 incident CV events and 1,289 deaths over approximately 9 years. Among persons without and with ADL limitation, SBP was directly associated CVD events, and the size of the HRs was similar in the two groups: HR (per 10 mmHg increase) 1.08 (95% CI 1.03, 1.13) and 1.06 (0.97, 1.17), respectively. ADL modified the association of DBP with incident CVD. Among those without ADL limitations, DBP was weakly associated with CVD, HR 1.04 (0.79, 1.37) for DBP > 80 compared to < 65. In contrast, among those with ADL limitation, DBP was inversely associated with CVD events. HR 0.65 (0.44, 0.96) for DBP 66-80 mmHg and HR 0.49 (0.25, 0.94) for DBP > 80 mmHg, compared to DBP ≤ 65 mmHg. Among persons with ADL limitation, a DBP 66-80 had the lowest risk for death, HR 0.72 (0.57, 0.91), compared with DBP ≤ 65 mmHg. Associations of BP with CVD or death did not vary by 15 feet walking speed.

Conclusions: ADL can identify the subgroups of elders in whom diastolic hypotension is associated with higher CV risk and death. Functional status, rather than chronologic age, should inform design of trials to elucidate benefits and harms of lowering each BP component in elders.

Introduction

Elderly persons aged 75 and older represent the fastest growing age group in the U.S., and about 2/3 are living with high blood pressure (BP). ¹ Optimal management of hypertension in elderly persons remains an issue of active debate. ²-5 Some studies show that high blood pressure (BP) is a risk factor for cardiovascular events and death in elderly persons. 6.7 Other studies have showed that higher BP is associated with *lower* risk for death in some elders, particularly those >75 years. A meta-analysis of trials including persons aged ≥ 80 reported reduction of cardiovascular risk, but not death, from lowering blood pressure. However, trial participants may not be representative of the general elderly population, where there is large heterogeneity of health status. Reliable identification of elders in whom high BP is associated with increased risk for cardiovascular events and death, and are thus most likely to benefit from treatment, remains difficult. We recently showed that walking speed of a 6 meter (20 feet) walk, a measure of functional status, can differentiate subgroups of elders in whom the association of systolic BP with death is incremental, null or reversed. Whether measures of health or functional status modify the association of BP with incident cardiovascular events remains uncertain.

Additional concern over excessive lowering of BP, particularly diastolic blood pressure (DBP), in elderly persons poses another major challenge. Isolated systolic hypertension (high SBP with normal or low DBP) is the most common form of hypertension in the elderly. Some, but not all, studies including elderly persons have shown associations of lower DBP with higher risk for cardiovascular events and death. Whether measures of functional status can identify the elders in whom low DBP is associated with increased risk cardiovascular events and death has not been well established.

We designed this analysis to evaluate whether limitations in activities of daily living (ADL) and a short test for gait speed (15 feet) modify the association between SBP or DBP with cardiovascular events and death among elders participating in the Cardiovascular Health Study (CHS). We hypothesized that higher SBP and DBP would be associated with higher risk for incident CVD and death among healthy elders, but not among elders with functional limitations.

Methods

Participants

We included participants who completed the 7th follow-up visit of the Cardiovascular Health Study. Briefly, CHS initially recruited community-dwelling Black and White individuals aged > 65 years from Medicare eligibility lists in four US communities (Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh, Pennsylvania), in two waves from 1989 to 1993. At enrollment, participants were excluded if they were not expected to remain in the current community for three years or longer, were receiving treatment for cancer, or were unable to provide informed consent.¹⁷ For these analyses, the 7th follow-up visit was considered the baseline visit to maximize inclusion of persons age > 75 years. For analyses of all-cause death, we included all individuals with year 7 measures of blood pressure for a total sample size of 3,547. For analyses considering incident cardiovascular disease as the outcome, we excluded 1,189 persons with prevalent CVD¹⁸ or heart failure, for a total sample size of 2,358. All participants provided written informed consent; the institutional review boards of the University of Washington and the affiliated clinical centers approved the study.

Systolic and diastolic blood pressure

Participants were asked to fast for 8 to 12 hours overnight prior to the study visit. Trained study personnel obtained three seated blood pressure readings, and the average of the last 2 readings was recorded using standardized procedures.

Outcomes

Our first outcome of interest was incident cardiovascular event (CVD) over 10 years. Incident CVD was defined as having myocardial infarction, cardiac arrest, stroke, or cardiovascular death among persons without a known history of CVD or heart failure. All events were adjudicated by a CHS outcome-assessment committee. Cases of CVD events were ascertained from hospital records that included clinical histories, elevated cardiac enzyme levels, electrocardiographic changes, and brain imaging studies. More details on event adjudication have been previously published. ^{17,18} The second outcome of interest was death from all causes. Deaths were identified by a review of obituaries, medical records, death certificates, and the Centers for Medicare and Medicaid Services health care—utilization database for hospitalizations and from household contacts; 100 percent complete follow-up for ascertainment of mortality status was achieved.

Effect Modifiers

Self-report of limitations in the ability to perform activities of daily living (ADL) and walking speed using a 15-foot walk were chosen *a priori* as potential effect modifiers. Difficulty with ADL and slow gait speed have been previously shown to be strong predictors of adverse outcomes.^{19,20} Ability to perform ADLs was ascertained by questionnaire by asking if a person had difficulty with eating, transferring from bed to chair, mobility inside the home, dressing, bathing, and using the toilet.²¹ We categorized persons into those without limitation and those who reported limitation of at least one ADL. The time (in 0.1 second increments) required for a person to walk 15 feet at their usual pace was recorded using a stopwatch. Walking speed was recorded in

meters per second (m/s). We categorized persons as fast (≥ 1.0 m/s), medium (0.60 – 0.99 m/s) or slow (<0.60 m/s) walkers based on clinically relevant cutpoints and based the distribution of gait speed in CHS.

Covariates

Covariate data was obtained concomitantly with BP measures. Age, gender, race, income, education, and past or present smoking were ascertained by questionnaire. Height and weight were measured with participants wearing light clothing and no shoes. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Physical activity was estimated as kilocalories per week, and assessed by self-report. Fasting blood was collected and stored at −70°F until needed for the appropriate assays, including HDL cholesterol, triglycerides, glucose. Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation. Cystatin C was measured by means of a particle-enhanced immunonephelometric assay (N Latex Cystatin C, Dade Behring) with a nephelometer (BNII, Dade Behring) and calibrated to international standard. Diabetes was defined as a self-report of diabetes, the use of insulin or oral hypoglycemic agents or a fasting glucose ≥126 mg/dL. Prevalent cardiovascular disease was defined as having a history of coronary heart disease, heart failure or stroke, and these have been previously validated in CHS. ¹⁸ Use of anti-hypertensive medication was ascertained by a medication inventory interview.

Analyses

We first evaluated the characteristics of participants overall and by reported difficulty with ADL. We used *t* test or chi square test, as appropriate. We then evaluated the distributions of SBP and DBP separately, stratified by ADL status. We investigated the association of SBP and DBP (separately) with incident cardiovascular events, modeling the predictors as continuous (per

standard deviation increase) and in categories to allow modeling of non-linear associations, using multivariable Cox regression. Categories of SBP and DBP were established based on clinically relevant cutpoints and the distribution of the data in CHS. We examined events over 10 years of follow-up. Nested models are presented as demographic adjusted (age, gender, race, education), followed by full adjustment for potential confounders and treatment with anti-hypertensive medications. We evaluated effect modification by stratifying *a priori* by ADL status and walking speed categories (slow, intermediate, fast) and calculating strata-specific hazard ratios. We also tested for a statistical interaction of SBP and DBP categories by ADL and walking speed (separately) for incident CVD, using the likelihood ratio test in fully adjusted models. As an exploratory analysis, we estimated incident CVD event rates stratified by both ADL status and anti-hypertensive treatment.

We were then interested in understanding the associations of combinations of SBP and DBP with risk of incident CVD. We categorized participants into four mutually exclusive categories that represent clinically relevant cutpoints for elderly persons and to mirror the categorizations above: (a) SBP \geq 150 & DBP > 65, (b) SBP \geq 150 & DBP \leq 65, (c) SBP < 150 & DBP \leq 65, and (d) SBP < 150 & DBP > 65. We evaluated the age-adjusted rates of events in each category. We then compared the association of each category with the referent (SBP < 150 & DBP > 65) for incident CVD using Cox proportional hazards, adjusting for demographic variables and confounders, stratified by ADL status. As secondary analyses, we also evaluated the association of pulse pressure with incident CVD, stratified by ADL status.

Results

Participant Characteristics

Among 3,547 elderly persons, the mean age was 78 ± 5 years, 61% were women, and 17% were African American. Approximately 21% (N=755) persons reported limitation in at least 1

ADL. In general, participants who reported having a limitation in ADL were older, more likely to be female, African American and have a lower level of education. Persons with ADL limitations were more likely to have known coronary heart disease and heart failure (CHF). (Table 1) The distributions of SBP and DBP were similar among persons with and without limitations in ADL (Figure 1). In the sub-cohort of persons included in the incident CVD analyses (N=2,459), the prevalence of ADL limitation was 18%. Similar to the larger cohort, persons with ADL limitation in this subset were also older, more likely to be women and had a higher prevalence of comorbidities.

Association of SBP and DBP with Incident CVD among persons without and with ADL limitation

Over a median follow-up time of 8.5 years, there were 631 and 147 incident CVD events in those without and with ADL limitation, respectively.

Among persons without and with ADL limitation, a higher SBP was incrementally associated with incident CVD, and the hazard ratios were similar among the two groups. (Table 2) Findings were similar when we used alternative cutpoints for SBP. For example, among persons without ADL limitation, the age-adjusted incident CVD rates were 34.4, 40.2, 50.3 and 58.9 for SBP <120, 120-139, 139-149, and ≥150, respectively.

When we examined the association of DBP with incident CVD, we found evidence of effect modification by ADL status. Among persons with no ADL limitation, higher DBP was associated with higher CVD risk, but results were not statistically significant after full adjustment. In contrast, among persons with ADL limitation, DBP was inversely associated with incident CVD. Compared to persons with DBP < 65 mmHg, those with DBP >80 and 66-80 mmHg had a 51% and 35% *lower* adjusted risk for incident CVD, respectively. (Table 2)

We then examined the association of combinations of SBP and DBP with incident CVD in persons with and without ADL limitation. Persons with SBP < 150 and DBP > 65 had the lowest rates of incident CVD across both ADL strata (Figure 2). Approximately 3.5% (N=125) of participants had very wide pulse pressures, with SBP ≥150 and DBP ≤ 65. While a relatively small group, these persons with widest pulse pressures had the highest age-adjusted rates of incident CVD within each strata of ADL. (Figure 2A and 2B)

Among persons without ADL limitation, a DBP \leq 65 did not confer any additional risk in persons with SBP <150, compared to persons with SBP < 150 and DBP > 65. (Figure 2A) However, among persons with ADL limitation, DBP \leq 65 was associated with a higher risk for incident CVD, whether the SBP was \leq or > 150, compared to the lowest risk group. Persons with SBP > 150 and DBP > 65 were at similar risk for incident CVD compared with persons with SBP < 150 and DBP > 65 among those with ADL limitation. (Figure 2B)

Finally, we examined the association of pulse pressure with incident CVD by ADL strata. Among persons without ADL limitation, there was no significant association between PP and incident CVD (HR 1.00 (0.92, 1.08) per 10 mmHg increase in PP). Among persons with ADL limitation, higher PP was significantly associated with higher risk for incident CVD, HR 1.17 (1.01, 1.34) per 10 mmHg increase in PP, p-value for interaction 0.37.

As an exploratory analysis, we estimated incident CVD rates for each BP category, stratified by both ADL status and anti-hypertensive treatment. Persons with higher SBP had higher rates of incident CVD, regardless of ADL limitation or treatment status. Among persons without ADL limitation, persons with DBP >80 had the highest rates of incident CVD, and the rates were similar for DBP ≤ 65 and 66-80 mmHg in both treated and untreated persons. In contrast, among persons with ADL limitation, there was an inverse gradient of DBP with incident CVD among those on treatment; the incident CVD rates were 96.6, 57 and 42.7, respectively for DBP

≤ 65, 66-80, >80 mmHg. Among persons with limitation and not on treatment, rates were 47.6 and 41.8 for DBP ≤65 and 66-80, respectively. There were too few persons (N=11) with a DBP > 80 mmHg in this group for precise comparisons.

Association of SBP and DBP with Mortality in persons with or without ADL limitation

There were 1289 and 498 deaths among participants without and with limitation in ADL, respectively. We did not appreciate strong associations between SBP and mortality, and findings did not vary by ADL status. (Table 3)

Among persons without limitation in ADL, a higher DBP was modestly associated with increased risk for death. Among persons with limitation in ADL, compared to persons with DBP \leq 65, those with DBP 66-80 had a 28% lower risk for death. Persons with DBP >80 had similar risk compared to persons with DBP \leq 65. (Table 3)

Association of BP with incident CVD and Mortality by walking speed

The association of SBP and DBP with incident CVD did not vary by strata of walking speed. (Table 4) Findings did not vary by walking speed for the total mortality outcome (all p-values >0.20). Only 206 persons (5.8%) had missing data on walking speed. There was no association between SBP or DBP with either outcome among persons with missing gait speed (data not shown).

Discussion

In this cohort of community-dwelling elders, we found that ADL status modifies some of the associations between blood pressure components and incident CVD and death. Specifically, among persons who do not report limitation in ADL, a higher SBP and DBP were associated with a higher risk for incident CVD. Among persons with ADL limitation, a high SBP remained associated with higher risk for incident CVD, whereas the association of DBP with CVD was

inverted. Moreover, among persons with ADL limitation, the combination of a high SBP and a low DBP conferred the highest risk for incident CVD, and pulse pressure was significantly and incrementally associated with CVD risk. A low DBP was also associated with a higher risk for death among persons with ADL limitation. Our findings suggest that functional status, assessed by ADL limitation, can inform understanding associations of BP components with incident CVD and death in elderly persons.

This study extends our prior reports showing that markers of functional status modify the association between blood pressure and death in elderly persons. ^{12,22} In addition, our findings shed light on the reasons for the inconsistent reports and current controversy on optimal BP levels in elderly persons. Observational studies have been conflicting on the association of high blood pressure with adverse outcomes in elderly persons. ^{6-9,23} A recent meta-analysis of randomized showed that treated elders had lower cardiovascular risk compared to untreated persons. However, there was large heterogeneity in the trials, and trial participants are unlikely to represent the general population of elders. ^{10,11} Our findings that a high SBP is significantly and incrementally associated with higher cardiovascular risk in persons without ADL limitation support the notion that lowering of SBP is beneficial in nonfrail elders. ^{24,25}

The findings that the associations of DBP with CVD and death were inverted among persons with ADL limitation are noteworthy. Isolated systolic hypertension (high SBP with low or normal DBP) is the most common form of hypertension in elders. The Systolic Hypertension in Elderly Program (SHEP) showed a benefit of lowering SBP in persons with isolated systolic hypertension. However, some studies have documented a J-shaped association of DBP with death and cardiovascular outcomes, but the importance of diastolic hypotension has been inconsistent across studies. He indings have led to concern that attempts to lower SBP can result in excessive DBP lowering and increased risk for adverse events in elderly persons. Our findings suggest that ascertaining limitation in ADL, rather than relying on

chronologic age alone, can identify the subgroup of elders in whom a low DBP is associated with a significantly higher risk for incident CVD and death. Our report that persons with ADL limitation and widest pulse pressure had the highest risk for incident CVD highlights the need for further investigation on the importance of the combined association of SBP and DBP with CVD risk and death in frail elders.

Reasons to explain why limitation in ADL may modify the association of DBP with incident CVD are not known. Some have suggested that elders with ADL limitation may represent a subgroup of ill persons who already have lower DBP, a marker of poor cardiovascular function. However, we found that DBP distributions did not vary by ADL limitation, and adjustment for confounders did not explain observed differences. It is also possible that limitation in ADL identifies persons with poor vascular tone and high degrees of vascular stiffness and who may be more susceptible to adverse effects of treatment. Adjustment for treatment did not affect our findings. Some, but not all, reports from randomized trials have suggested that on-treatment diastolic hypotension is associated with higher risk for CVD and death. 14,15,27 Few studies have examined whether existing vascular dysfunction in frail elders explains the association of diastolic hypotension with adverse outcomes. Finally, some suggest that differences in functional status may identify the elders who are aging successfully vs. those who are "dying". It is possible that aggressive attempts to lower SBP in a "dying" elder may increase the risk for adverse outcomes associated with diastolic hypotension. Future studies are needed to describe the associations of blood pressure trajectories with CVD and mortality risk.

Our report represents a large, heterogeneous, well-characterized cohort of community-dwelling elders. Our study is observational in nature, and thus limited in inferring causality. However, no large randomized trials including frail elderly persons has been conducted to accurately investigate benefits and harms of lowering SBP or DBP in this group. We have limited power to explore specific treatment effects as additional effect modifiers. We are also limited in our ability

to explore a larger number of combinations of SBP and DBP. However, our findings using clinically relevant cutpoints support those observed for each BP component alone. We found that speed to complete a 15-ft walk did not modify the association of BP with outcomes. Longer walk distances may be required to elucidate relevant subgroups. Our findings highlight the urgency of including frail elders in trials of hypertension treatment. Our data suggest that patient characteristics (such as functional and health status) may be more informative in ascertaining optimal BP levels in elderly persons, rather than chronologic age alone.

In summary, we found that knowledge of an elder's ability to perform ADLs may improve our understanding of the association of SBP and DBP with CVD risk and death. Among persons without ADL limitation, a lower SBP is associated with lower cardiovascular risk, and a wider range of DBP (and thus pulse pressure) may be acceptable. In contrast, among persons with limitation in ADL, the benefit of a lower SBP may need to be weighed against the associations of diastolic hypotension with higher risk for CVD and death. Future research is necessary to determine benefits and harms of lowering each BP component in frail adults, and the role of vascular stiffness in explaining these observations.

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Table 1. Characteristics of 3,547 elders in CHS by Ability to Perform ADL

	Total	No Limitation in ADL	Limitation in ≥ 1 ADL
N	3547	2792	755
Age	78 (5)	78 (5)	80 (6)
Female	2150 (61%)	1622 (58%)	528 (70%)
African American	584 (17%)	430 (15%)	154 (20%)
Education			
None-grade 9	555 (16%)	392 (14%)	163 (22%)
HS graduate	1317 (37%)	1053 (38%)	264 (35%)
Professional	1667 (47%)	1344 (48%)	323 (43%)
Smoking			
Former	1536 (44%)	1220 (45%)	316 (43%)
Current	259 (8%)	209 (8%)	50 (7%)
Physical activity kcal/wk*	675 [183, 1598]	795 [270, 1755]	296 [0, 945]
BMI, kg/m ²	26.9 (4.7)	26.6 (4.4)	28.3 (5.5)
SBP	137 (21)	137 (21)	138 (21)
DBP	70 (11)	70 (11)	70 (12)
Treated with anti- hypertensives	2074 (59%)	1588 (57%)	486 (65%)
Diabetes	529 (16%)	382 (14%)	147 (22%)
Total cholesterol	202 (40)	201 (40)	204 (40)
Cystatin C	1.16 (0.41)	1.14 (0.37)	1.27 (0.53)
History of CHD [¥]	885 (25%)	656 (24%)	229 (30%)
History of CHF [*]	354 (10%)	218 (8%)	136 (18%)

BMI= body mass index, CHD= coronary heart disease, CHF=congestive heart failure

^{*}median [IQR] ¥ Excluded for the incident CVD analyes

Table 2. The Association of SBP and DBP with Incident CVD stratified by ADL

	N	Rate per 1000 PY	Demo Adjusted* HR (95% CI)	Adjusted** HR (95% CI)
		SBP		
Without ADL Limitation				
SBP (per 10 mmHg increase)	1943	44.5	1.08 (1.04, 1.12)‡	1.08 (1.03, 1.13)‡
≤ 120	380	34.3	1.00	1.00
121 – 150	1146	43.1	1.24 (0.99, 1.57)	1.20 (0.94, 1.52)
> 150	417	58.7	1.54 (1.19, 2.01)†	1.48 (1.11, 1.98)†
With ADL Limitation	717	30.7	1.04 (1.10, 2.01)	1.40 (1.11, 1.50)
SBP (per 10 mmHg	415	56.9	1.03 (0.95, 1.13)	1.06 (0.97, 1.17)
increase) SBP				
≤ 120	71	39.4	1.00	1.00
121 – 150	240	56.3	1.38 (0.81, 2.33)	1.62 (0.94, 2.79)
> 150	104	72.7	1.45 (0.80, 2.63)	1.72 (0.91, 3.26)
		DBP		
Without ADL Limitation				
DBP (per 10mmHg	1946	30.4	1.07 (0.99, 1.15)	1.00 (0.93, 1.09)
increase)	1340	30.4	1.07 (0.99, 1.13)	1.00 (0.93, 1.09)
DBP				
≤ 65	602	43.8	1.00	1.00
66 – 80	1028	41.9	1.02 (0.85, 1.23)	0.94 (0.7, 1.14)
> 80	313	55.1	1.26 (0.99, 1.61)	1.04 (0.79, 1.37)
With ADL Limitation	313	33.1	1.20 (0.33, 1.01)	1.04 (0.73, 1.37)
DBP (per 10mmHg	415	56.9	0.87 (0.74, 1.02)	0.85 (0.73, 1.00)
increase) DBP	413	50.9	0.07 (0.74, 1.02)	0.00 (0.70, 1.00)
	134	71.7	1.00	1.00
≤ 65 66 – 80	211	71.7 51.8	0.70 (0.48, 1.03)	0.65 (0.44, 0.96)†
> 80	70	45.5	0.60 (0.33, 1.09)	0.49 (0.25, 0.94)†
*adjusted for age, gonder			0.00 (0.33, 1.09)	0.73 (0.23, 0.34)

^{*}adjusted for age, gender, race and education
** Further adjusted smoking, physical activity, BMI, DM, total cholesterol, cystatin C and HTN meds and SBP or DBP, respectively. P-value for interactions SBP*ADL=0.23, DBP*ADL=0.18.

[†] p<0.05

[‡] p<0.001

Table 3. The Association of SBP and DBP with All-Cause Mortality stratified by ADL

			Demo	Adjusted**
	N	Rate per 1000 PY	Adjusted* HR (95% CI)	HR (95% CI)
		SBP		
Without ADL Limitation				
SBP (per 10 mmHg	2792	58.5	0.99 (0.96, 1.02)	0.97 (0.94,0.99)†
increase)				
SBP	E07	60.8	1.00	1.00
≤ 120 121 – 150	587 1587	56.2	0.87 (0.75, 1.00)	0.88 (0.76, 1.03)
> 150	618	62.3	0.90 (0.76, 1.07)	0.83 (0.68, 1.00)
With ADL Limitation	010	02.3	0.90 (0.70, 1.07)	0.03 (0.00, 1.00)
SBP (per 10 mmHg	755	102.9	1.01 (0.96, 1.06)	1.01 (0.96, 1.06)
increase)	700	102.0	1.01 (0.00, 1.00)	1.01 (0.00, 1.00)
SBP				
≤ 120	130	107.5	1.00	1.00
121 – 150	450	93.7	0.83 (0.62, 1.10)	0.94 (0.70, 1.25)
> 150	175	125.4	1.07 (0.77, 1.48)	1.12 (0.80, 1.58)
		DBP		
Without ADL Limitation				
DBP (per 10mmHg	2792	58.5	0.98 (0.93, 1.03)	1.07 (1.01,1.14)†
increase)				
DBP				
≤ 65	941	63.6	1.00	1.00
66 – 80	1425	55.0	0.94 (0.83, 1.07)	1.11 (0.97, 1.27)
> 80	426	59.4	0.99 (0.83, 1.18)	1.30 (1.06,1.61)†
With ADL Limitation		400.0	0.00 (0.04 4.55)	0.07 (0.00 4.57)
DBP (per 10mmHg	755	102.9	0.93 (0.84, 1.02)	0.97 (0.88, 1.07)
increase)				
DBP	050	420.0	1.00	1.00
≤ 65 66 90	258	120.8	1.00	1.00
66 – 80 > 80	366 121	86.7 120.7	0.68 (0.54,0.86)†	0.72 (0.57,0.91)†
> 80	131	120.7	0.87 (0.63, 1.20)	0.87 (0.61, 1.24)

^{*}adjusted for age, gender, race and education
** Further adjusted smoking, physical activity, BMI, DM, total cholesterol, cystatin C and HTN meds and SBP or DBP, respectively. P-value for interaction SBP*ADL=0.55, DBP*ADL=0.23

[†]p<0.05

[‡] p<0.001

Table 4. Association of SBP and DBP with incident CVD across strata of walking speed

			Demo Adjusted*	Adjusted**			
	N	Rate per 1000 PY	HR (95% CI)	Aujusteu			
		Incident CVD					
SBP							
		alking speed <0.60					
SBP (per 10 mmHg increase)	303	81.6	1.07 (0.97, 1.18)	1.06 (0.96, 1.17)			
SBP							
≤ 120	56	66.7	1	1.00			
121 – 150	174	80.8	1.26 (0.69, 2.32)	1.25 (0.67, 2.35)			
> 150	73	97.6	1.49 (0.79, 2.92)	1.43 (0.69, 2.93)			
	Walk	ing speed 0.60 – 0.	99				
SBP (per 10 mmHg increase)	1391	52.2	1.10 (1.05, 1.15)‡	1.10 (1.05, 1.16)‡			
SBP							
≤ 120	243	41.7	1	1.00			
121 – 150	826	48.2	1.19 (0.91, 1.57)				
> 150	322	71.5	1.67 (1.23, 2.25)‡	1.81 (1.30, 2.51)‡			
		alking speed ≥ 1.00	, , , , , , , , , , , , , , , , , , , ,	(, , , , ,			
SPD (per 10 mmHg increase)				1.07 (0.00, 1.16)			
SBP (per 10 mmHg increase)	717	37.8	1.06 (1.00, 1.13)	1.07 (0.99, 1.16)			
SBP							
≤ 120	163	28.3	1	1.00			
121 – 150	412	40.7	1.43 (0.98, 2.07)	1.37 (0.94, 2.04)			
> 150	142	41.0	1.38 (0.88, 2.16)	1.36 (0.82, 2.24)			
		DBP					
	W	alking speed <0.60					
DBP (per 10 mmHg increase) DBP	303	81.6	1.01 (0.84, 1.21)	0.94 (0.79, 1.13)			
≤ 65	108	71.3	1	1.00			
66 – 80	138	90.1	1.27 (0.81, 1.99)	1.07 (0.66, 1.72)			
> 80	57	81.1	0.93 (0.48, 1.81)	0.66 (0.31, 1.38)			
	Walk	ing speed 0.60 – 0.	99				
DBP (per 10 mmHg increase)	1391	52.2	1.04 (0.95, 1.13)	0.99 (0.90, 1.08)			
DBP			, ,	, ,			
≤ 65	433	55.1	1	1.00			
66 – 80	752	46.9	0.89 (0.73, 1.10)	0.85 (0.68, 1.05)			
> 80	117	66.0	1.29 (0.99, 1.69)	1.09 (0.80, 1.48)			
	Wa	alking speed ≥ 1.00					
DBP (per 10mmHg increase)	717	37.8	1.00(0.88, 1.14)	0.93 (0.80, 1.07)			
DBP							
	213	41.9	1	1.00			
66 – 80	387	36.6	0.93 (0.68, 1.27)	0.81 (0.58, 1.14)			
> 80	117	34.9	0.83 (0.54, 1.28)	0.62 (0.37, 1.03)			
			, , ,	, , ,			

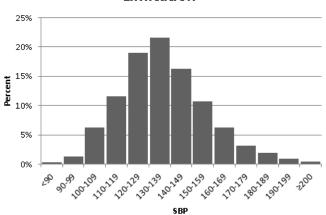
*adjusted for age, gender, race and education
** Further adjusted smoking, physical activity, BMI, DM, total cholesterol, cystatin C and HTN meds and SBP or DBP, respectively. P-value for interaction SBP*walk=0.70, DBP*walk=0.59

† p<0.05 ‡ p<0.001

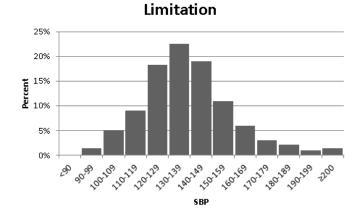
Figure 1. Distribution of SBP and DBP among CHS Participants with and without ADL limitation

Panel A: SBP and DBP among persons without ADL limitation

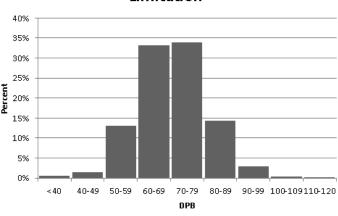




Panel B: SBP and DBP among persons with ADL limitation ≥1
SBP Among Persons with ADL≥1



DBP Among Persons Without ADL Limitation



DPB Among Persons With ADL≥1 Limitation

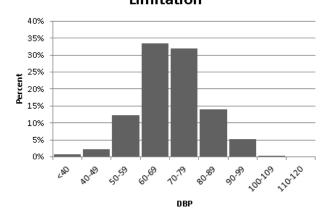


Figure 2: The Association of Combined SBP and DBP Categories with Incident CVD with and without ADL limitation

Without ADL limitation	N	Age-Adjusted Rate (%/yr)	Low Risk High Risk	
SBP < 150 & DBP > 65	974	4.1		
SBP < 150 & DBP ≤ 65	575	4.4		
SBP ≥ 150 & DBP > 65	404	6		
SBP ≥ 150 & DBP ≤ 65	56	7.6	-	
				3
			0.50 1.50 2. *HR (95%CI)	.50

With ADL limitation	N	Age-Adjusted Rate (%/yr)	Low Risk	High Risk	
SBP < 150 & DBP > 65	204	4.7		•	
SBP < 150 & DBP ≤ 65	121	6.8	+	- I	
SBP ≥ 150 & DBP > 65	104	6	-	<u> </u>	
SBP ≥ 150 & DBP ≤ 65	21	13.3	1		
			0.50	1.50	2.50
				IR (95%CI)	

^{*}adjusted for age, gender, race and education