Published in final edited form as:

J Am Geriatr Soc. 2017 July ; 65(7): 1482–1489. doi:10.1111/jgs.14816.

Functional Status Modifies the Association of Blood Pressure with Death in Elders: Health and Retirement Study

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Abstract

Objective—To examine whether grip strength, gait speed, and the combination of the two physical functioning measures modified the association of systolic BP (SBP) and diastolic BP (DBP) with mortality.

Design—Nationally representative cohort study.

Setting—Health and Retirement Study.

Participants—7492 U.S. adults aged ≥ 65 years.

Measurements—Grip strength was measured by a hand dynamometer and classified as normal (≥ 16 kg for female; ≥ 26 kg for male) and weak. Gait speed was assessed over a 98.5-inch walk and classified as non-slow (≥ 0.60 m/s for female; ≥ 0.52 m/s for male) and slow.

Results—Over an average follow-up time of 6.0 years, 1870 (25.0%) participants died.

After adjustment for socio-demographic, behavioral, and clinical measures, elevated SBP (≥ 150 mmHg) and DBP (≥ 90 mmHg) was associated with a 24% (95%CI, 7%, 43%) and 25% (95%CI, 5%, 49%) higher mortality among participants with normal grip strength. In contrast, elevated SBP and DBP was associated with a 6% (95% CI, 31%, –27%) and a 16% (95%CI, 46%, –26%)

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An abstract of this study was presented at the Society for Epidemiologic Research, Miami, FL, 2016.

Authors' contributions: Study concept and design: CW, CAP, MCO. Analysis and interpretation of data: CW, ES, MCO. Subject matter expertise: CAP, HS, MCO. Preparation, revision, and approval of manuscript: CW, ES, CAP, HS, MCO. Chenkai Wu had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of interest: The authors have no conflicts of interest to disclose relevant to this article.

SUPPLEMENTARY MATERIAL

Supplementary Table S1. Characteristics of Adults Aged at Least 65 Years across the Combination of Grip Strength and Gait Speed.

Supplementary Table S2. Association of Blood Pressure with Mortality among Participants Who Did Not Complete the Grip Strength Test Due to Non-Logistical Reasons.

Supplementary Table S3. Association of Blood Pressure with Mortality by Gait Speed.

Supplementary Table S4. Association of Systolic Blood Pressure (vs. < 140 mmHg) with Mortality by the Combination of Grip Strength and Gait Speed

lower mortality among those with weak grip strength (*P-values* of interactions: both=.07). The inverse relations between BP with death were most pronounced among slow walkers with weak grip strength. The HRs of elevated SBP and DBP for death were 0.85 (95%CI, 0.56–1.29) and 0.53 (95%CI, 0.30–0.96), respectively, and were substantially different from non-slow walkers with normal grip strength (HR=1.24 and 1.15, respectively; *P-values* of interactions: both<.001). Associations of BP with death varied modestly by gait speed.

Conclusion—Grip strength modified the association of BP with death. Combination of grip strength and gait speed has incremental value for modifying the association of BP with death.

Keywords

blood pressure; grip strength; gait speed; mortality

INTRODUCTION

Older adults represent the fastest growing age group in the U.S. and have the highest prevalence of hypertension.¹ Although the majority of evidence points toward an increase in cardiovascular morbidity and mortality among persons with high blood pressure (BP), the findings are less clear among some populations of older adults, especially frail/low-functioning persons or the very old. There has been a large body of epidemiological evidence showing low BP is associated with increased risk of cardiovascular (CV) events, poor physical and cognitive functions, and mortality in elders;^{2–11} whereas other studies have reported elevated BP remains to be a risk factor for CV outcomes and mortality in old age.^{12,13} Moreover, findings from randomized controlled trials (RCTs) are mixed with regard to the benefits of antihypertensive treatment in reducing mortality among older adults,^{14–20} the optimal treatment for hypertension in this age group remains controversial.^{21–25}

Reasons for these differences in the association of high BP with death among elders are largely unknown. One explanation is substantial heterogeneity exists in health status among older adults; there may exist subgroups of elders who are not at increased risk for high BP-related death. We have previously demonstrated the association of high BP with mortality was attenuated in low-functioning elders, characterized by slow gait speed at usual pace.^{26,27} However, whether other functional measures modify this relationship is less well known. Grip strength, an indicator of overall body strength,²⁸ is an ideal alternative marker. Grip strength is a key component of frailty,²⁹ and is associated with cognitive decline,³⁰ disability,³¹ and mortality.³² Moreover, grip strength is frequently available in epidemiological studies and can be conveniently assessed by a simple and inexpensive device in the clinical setting.

We examined whether grip strength and gait speed modified the associations of systolic BP (SBP) and diastolic BP (DBP) with mortality among older adults. Based on existing findings,^{26,27,33–38} we hypothesized that higher SBP and DBP would be each associated with increased mortality among adults with normal functional status, but these associations would be attenuated in low-functioning ones. We also investigated the incremental value of

grip strength in combination with gait speed in identifying older adults who are not at increased risk of high BP-related mortality.

METHODS

Study Design

The Health and Retirement Study (HRS) is a population-based cohort study of a nationally representative sample of non-institutionalized adults aged ≥ 51 years in the U.S. The HRS was launched in 1992 and had assessments on health conditions, financial situation, and employment status every other year thereafter. In Wave 2006, approximately 50% of the participants were randomly selected to participate in an enhanced face-to-face interview, during which BP, physical function, and blood-based biomarkers were measured. The other half of the sample completed the functional measures and biomarkers in Wave 2008. The study protocol was approved by the University of Michigan Institutional Review Board. Further details about the recruitment strategies, study designs, and sampling approaches of the HRS have been documented elsewhere.³⁹

Participants

We used pooled data from the 2006 and 2008 waves. The sample was restricted to 7500 participants who (a) aged ≥ 65 years, (b) had ≥ 1 BP reading obtained in a sitting position with full compliance, (c) completed grip strength and gait speed measures, and (d) had mortality information. Eight participants with extreme gait speed (>2.0 m/s) were further excluded.

Outcome

The outcome was all-cause mortality. Vital status and date of death were ascertained based on a variable that recorded participants' year and month of death taken from the respondent's exit interview or the spouse/partner's interview. Mortality status was ascertained through April 2015. Participants were censored when lost to follow-up or the end of the analytic period (April 2014).

Predictors

BP was measured by trained interviewers using automated sphygmomanometer. Three BP readings, 45–60 seconds apart, were taken in a sitting position with both feet on the floor and the left arm supported with the palm facing up.⁴⁰ The average of the readings was calculated.

Effect Modifiers

Grip strength (kg) was measured by a spring-type hand dynamometer. Participants were asked to squeeze the meter at their maximum capacity in a standing position twice for each hand. The average of readings for dominant hand was calculated. For participants who reported having equally strong hands, the higher average was used. Based on clinically relevant cut-points suggested by Alley et al,⁴¹ a grip strength <16 kg for female and <26 kg for male was classified as "weak". Gait speed was calculated by converting the amount of

time required to walk 98.5 inches (≈ 2.5 meters) at usual pace into meter per second. Two trials were conducted, and the average was calculated. We used the lowest quintile of the sample distribution as cut-point to classify slow (<0.52 m/s for female; <0.60 m/s for male) and non-slow walkers.

Covariates

Demographics included age, sex, race (white, non-white), and education ($<$ high school, high school, $>$ high school). Behavioral characteristics included smoking status (current, former, never), and body mass index (BMI) defined as body weight (kilograms) divided by height (meters) squared. Clinical measures included total cholesterol, high-density lipoprotein (HDL) cholesterol, glycosylated hemoglobin (HbA1c), C reactive protein (CRP), and cystatin C; missing clinical measures were imputed using the last-observation-carried-forward approach. Chronic conditions including cardiac disease, stroke, cancer (excluding skin cancer), diabetes (assessed by self-report, medication use, or insulin use), lung disease, and arthritis and antihypertensive medication use (yes, no) were self-reported.

Statistical Analysis

We first compared participants across grip strength and gait speed (separately) using a chi-squared test for categorical variables and a t-test for continuous variables. We estimated the mortality rates across grip strength (weak vs. normal) and gait speed (slow vs. non-slow); we then calculated the risk difference in persons with and without elevated BP (≥ 150 mmHg for SBP; ≥ 90 mmHg for DBP) across grip strength and gait speed.

We used Cox models⁴² to estimate the association of SBP and DBP (separately) with mortality. SBP and DBP were modeled both as continuous variables (per 10-mmHg) and in categories (<150 and ≥ 150 mmHg for SBP; <90 and ≥ 90 mmHg for DBP).²² Demographics, behavioral measures, clinical measures, medical history, and antihypertensive medication were included as covariates in adjusted models. We used robust standard errors to account for the nested data structure of the HRS.

To evaluate effect modification, we included interactions between grip strength and gait speed and elevated BP and used a Wald test for interaction. We then stratified the models by categories of grip strength and gait speed. The joint effect of grip strength and gait speed was examined by entering the terms for the combination of grip strength and gait speed; we used a global test for interaction to examine whether the association of BP with death varied by functional status.

We conducted several sensitivity analyses. First, we evaluated the association of BP with mortality by functional status, excluding deaths that occurred in the first two years of follow-up ($n=413$). Additionally, we repeated the analyses with a different cutoff for defining elevated SBP (≥ 140 mmHg). Lastly, because not completing the physical function test may be an indicator of low functional status, we examined the association of BP with mortality among participants who did not complete the walk and grip strength tests due to reasons other than logistical (separately). All analyses were performed using Stata 13.1.⁴³

RESULTS

Participant Characteristics

Over an average follow-up time of 6.0 years, 1870 participants died; the mortality rate was 41.5 per 1000 person-years (PYs). A total of 1077 (15.9%) participants were classified as “weak” in grip strength. The average BP levels for participants with weak and normal grip strength were 133.3 and 134.5 mmHg (SBP), and 76.1 and 76.8 mmHg (DBP), respectively (Table 1). Participants with weak grip strength were older, less likely to be male, had fewer years of education than those with normal grip strength. Persons with weak grip strength also had higher prevalence of a history of cardiac disease, stroke, diabetes, cancer, lung disease, arthritis, and antihypertensive medication. Participants with the lowest physical function (weak grip strength and slow gait speed) were older and more likely to be women, had higher prevalence of chronic conditions than those with either normal grip strength or non-slow gait speed or both (Supplementary Table S1). They also had lower levels of total cholesterol and HDL cholesterol and higher levels of cystatin C and CRP.

Association of BP with Mortality across Grip Strength

Mortality rates were 35.4 and 85.4 per 1000 PYs among participants with normal and weak grip strength, respectively. Among those with weak and normal grip strength, the differences in mortality rates between SBP ≥ 150 and <150 mmHg were 9.3 and 14.7 per 1000 PYs, respectively (Table 2). The difference in mortality rate between DBP ≥ 90 and <90 mmHg was 2.4 per 1000 PYs for persons with normal grip strength, whereas weak participants with high DBP (≥ 90 mmHg) had a lower mortality rate (-9.8 per 1000 PYs).

There is suggestive evidence that the association of high SBP (≥ 150 mmHg) and mortality differed across grip strength; *P*-values of interactions for unadjusted and adjusted models were 0.03 and 0.07, respectively. After multivariable adjustment, higher SBP was associated with a 24% higher mortality among persons with normal grip strength ($P<0.01$). In contrast, SBP was not associated with mortality among weak participants; the HR was 0.94 (95% CI, 0.69–1.27). The adjusted HR for high DBP (≥ 90 mmHg) was 1.25 (95% CI, 1.05–1.49) among participants with normal grip strength, whereas weak participants with high DBP had a lower mortality risk, although the relation was not significant (HR, 0.84; 95% CI, 0.56–1.26). *P*-values of interactions for unadjusted and adjusted models of DBP were 0.26 and 0.07, respectively. We did not find that higher BP was associated with lower mortality among 225 non-completers of the grip strength test (Supplementary Table S2).

Association of BP with Mortality across Gait Speed

The differences in mortality rates between SBP ≥ 150 and <150 mmHg were 9.1 and 13.4 per 1000 PYs for slow and non-slow walkers, respectively (Supplementary Table S3). Slow walkers with elevated DBP had a lower mortality rate (-3.4 per 1000 PYs), whereas the difference in mortality rate between DBP ≥ 90 and <90 mmHg was 0.7 per 1000 PYs among non-slow walkers. After multivariable adjustment, the HR of higher SBP (≥ 150 mmHg) for death was not significantly higher among slow walkers, whereas higher SBP was associated with a significantly higher mortality among non-slow walkers (HR, 1.17; 95% CI, 1.00–1.38); *P*-value for interaction=0.36. The association of DBP with mortality did not vary

substantially by gait speed. An inverted relationship was observed between elevated SBP and mortality among 483 non-completers of the walk test due to non-logistical reasons (Supplementary Table S3).

Association of BP with Mortality across the Combination of Grip Strength and Gait Speed

We investigated the joint effect of grip strength and gait speed with the reference being normal grip strength and non-slow gait speed. The associations of SBP and DBP with death varied by functional status (P -values of global tests for interactions <0.001). Among slow walkers with weak grip strength (poor functioning; $n=458$, 6.1%) and non-slow walkers with normal grip strength (usual functioning; $n=5375$, 71.7%), the mortality associated with elevated SBP was 0.85 and 1.24, respectively (Table 3). The mortality related to elevated DBP among slow walkers with weak grip strength was much lower than those who had non-slow gait speed and normal grip strength (HR=0.53 vs 1.15).

Sensitivity Analyses

Results were robust against sensitivity analyses where participants who died within the first two years were excluded. The association of elevated SBP and DBP with death differed between participants with low and normal grip strength; P values for interactions were 0.02 and 0.01, respectively (Table 4). In contrast, the associations were not significantly modified by gait speed. The inverse relation between BP and death was most pronounced among participants having weak grip strength and slow gait speed (Figure 1). Additionally, results did not change substantially when elevated SBP was defined based on an alternative cut-point (>140 mmHg) (Supplementary Table S4).

DISCUSSION

In this nationwide cohort study of 7492 U.S. older adults, we found grip strength modified the association of BP with death. Specifically, among elders with normal grip strength (>16 kg for female; >26 kg for male), elevated SBP (>150 mmHg) and DBP (>90 mmHg) were associated with increased mortality risk, whereas there were no significant relationships among those with weak grip strength. However, evidence is less consistent for gait speed. Moreover, we found that the inverse associations of BP with mortality were most pronounced among participants with weak grip strength and slow gait speed.

Our findings are consistent with prior studies showing that the association of high BP with CV events and mortality was attenuated or inverted in elders with poor functional status.^{26,27,33–36,38} We extended previous research by examining the role of grip strength, an indicator of overall body strength and physical function,²⁸ in the association of BP with death. Our findings suggest, compared to gait speed, grip strength may be a better marker of functional status in identifying subgroups of older adults in whom low BP is potentially beneficial. Previous investigations into gait speed as an effect modifier of the association of BP with outcomes have been mixed. While majority of evidence points towards a gait speed as a strong effect modifier, one previous study reported no effect modification by gait speed. Peralta et al.³⁴ found that the association of BP with cardiovascular disease or death varied by limitation in performing activities of daily living but not by gait speed among adults aged

75 years. One reason for this inconsistency could be the variation of assessment of usual gait speed (e.g. distance, walking surface).^{44–46} It is also possible that other factors (e.g. habit, motivation) may influence gait speed, or that different measures may better capture effect modification across different populations. Interestingly, we found that elevated SBP was associated with a lower mortality in non-completers of the walk test, which is consistent with previous findings.²⁶ Walk test requires coordination of multiple physiological systems, and missingness on the walk test may be an indicator of a low level of overall functional status. In contrast, we did not find an inverse relation between BP with mortality among non-completers of the grip strength test. One explanation is missing data on the grip strength test may be an indicator for hand impairment rather than a reduced level of overall health, and therefore a poor surrogate for functional status. However, special caution is needed to interpret these results because there was a wide range of non-logistical reasons for not completing the test, precluding us from drawing definite conclusions.

In addition to examining the independent role of grip strength and gait speed in the relation between BP and death, we investigated two measures jointly. The association of low BP with higher mortality was most pronounced among slow walkers with weak grip strength. These findings suggest combination of grip strength and gait speed has incremental value for identifying low-functioning elders who are not at increased risk of high BP-related mortality. Functional status is a multidimensional construct encompassing functional capacity, performance, reserve, and capacity utilization.⁴⁷ Combining grip strength with gait speed, which capture different aspects of functional status, may better assess functional status and identify low-functioning persons compared to either measure alone.

The mechanisms by which functional status modifies the relation between high BP and death are not well understood. One possible explanation is, among elders with declined functional status, high BP is important for maintaining adequate perfusion of vital organs such as heart and brain,^{24,36,48} which may prevent increased risk of CV and cerebrovascular events. Several lines of evidence support this explanation. Sabayan et al. found higher SBP was associated with lower risk of incident stroke among cognitively impaired elders.²⁸ Peralta et al. showed that elevated DBP was related to a reduced risk of incident CV events.³⁴ Another explanation for the null association of BP with mortality among low-functioning adults is that low BP can be a marker for the end of life. However, the data suggest this is not plausible because similar patterns of association were observed when excluding persons who died within the first two years of follow-up.

Strengths of this study include a large, heterogeneous cohort of non-institutionalized elders, availability of multiple physical functioning measures, a relatively long follow-up period, and detailed data on demographic, behavioral, and clinical covariates. We acknowledge several limitations. First, we only used the baseline levels of BP and functional measures; these measures may vary over time, leading to misclassification. In addition, although we adjusted for a wide range of confounders, residual confounding could still exist. RCTs may minimize this unavoidable bias in observation studies. However, elderly patients in trials are selective due to stringent exclusion criteria; trial results may not be generalizable to the general elderly population. Recently, Bress et al.⁴⁹ showed that only 19.5% of U.S. adults aged 60–74 years and 34.6% aged 75 years were eligible for the Systolic Blood Pressure

Intervention Trial (SPRINT). A treatment de-intensification trial, where patients receive either standard treatment or a less intensive one, may provide a better understanding of the association of BP with mortality among low-functioning older adults, who are not well represented in clinical trials. Moreover, we focused on the modifying effects of two markers of physical function. However, we understand that the association of low BP with higher risk of unfavorable outcomes has also been observed among elders with impaired cognitive function^{35,36} and older patients with more advanced vascular age.^{48,50,51} Future research needs to evaluate whether combination of different markers of physical, cognitive, and vascular age could better identify elders who are vulnerable to low BP.

In a nationwide cohort of U.S. older adults, physical function measures modified the association of BP with death. The inverse associations of BP with mortality were most pronounced among participants with weak grip strength and slow gait speed. Findings are relevant to antihypertensive treatment decisions because findings of the SPRINT may result in more aggressive interventions among the general elderly population, which includes low-functioning elders. Moreover, our findings may further advance precision medicine, which emphasizes the importance of tailoring medical decisions and practices to individuals based on their genetic signature, clinical characteristics, and functional status.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study was supported by National Institute on Aging (K01AG039387, R01AG46206).

REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics-2015 update: a report from the American Heart Association. *Circulation*. 2015; 131(4):e29. [PubMed: 25520374]
2. Sabayan B, Oleksik AM, Maier AB, et al. High blood pressure and resilience to physical and cognitive decline in the oldest old: the Leiden 85-plus study. *J Am Geriatr Soc*. 2012; 60(11):2014–2019. [PubMed: 23126669]
3. Rastas S, Pirttilä T, Viramo P, et al. Association between blood pressure and survival over 9 years in a general population aged 85 and older. *J Am Geriatr Soc*. 2006; 54(6):912–918. [PubMed: 16776785]
4. Mossello E, Pieraccioni M, Nesti N, et al. Effects of low blood pressure in cognitively impaired elderly patients treated with antihypertensive drugs. *JAMA Intern Med*. 2015; 175(4):578–585. [PubMed: 25730775]
5. Molander L, Lövheim H, Norman T, Nordström P, Gustafson Y. Lower systolic blood pressure is associated with greater mortality in people aged 85 and older. *J Am Geriatr Soc*. 2008; 56(10):1853–1859. [PubMed: 18811610]
6. Hakala SM, Tilvis RS, Strandberg TE. Blood pressure and mortality in an older population. *Eur Heart J*. 1997; 18:1019–1023. [PubMed: 9183596]
7. Boshuizen HC, Izaks GJ, van Buuren S, Ligthart GJ. Blood pressure and mortality in elderly people aged 85 and older: community based study. *BMJ*. 1998; 316(7147):1780–1784. [PubMed: 9624064]
8. Abreo AP, Glidden D, Painter P, et al. Association of physical function with predialysis blood pressure in patients on hemodialysis. *BMC Nephrol*. 2014; 15(1):177. [PubMed: 25399253]

9. Mattila K, Haavisto M, Rajala S, Heikinheimo R. Blood pressure and five year survival in the very old. *BMJ*. 1988; 296(6626):887–889. [PubMed: 3129061]
10. Stroup-Benham CA, Markides KS, Black SA, Goodwin JS. Relationship between low blood pressure and depressive symptomatology in older people. *J Am Geriatr Soc*. 2000; 48(3):250–255. [PubMed: 10733049]
11. Rajala S, Haavisto M, Heikinheimo R, Mattila K. Blood pressure and mortality in the very old. *Lancet*. 1983; 322(8348):520–521.
12. Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet*. 2014; 383(9932):1899–1911. [PubMed: 24881994]
13. Prospective Studies C. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002; 360(9349):1903–1913. [PubMed: 12493255]
14. Bejan-Angoulvant T, Saadatian-Elahi M, Wright JM, et al. Treatment of hypertension in patients 80 years and older: the lower the better? A meta-analysis of randomized controlled trials. *J Hypertens*. 2010; 28(7):1366–1372. [PubMed: 20574244]
15. Beckett NS, Peters R, Fletcher AE, et al. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med*. 2008; 358(18):1887–1898. [PubMed: 18378519]
16. Gueyffier F, Bulpitt C, Boissel J-P, et al. Antihypertensive drugs in very old people: a subgroup meta-analysis of randomised controlled trials. *Lancet*. 1999; 353(9155):793–796. [PubMed: 10459960]
17. Moonen JEF, Bertens AS, Foster-Dingley JC, et al. Lower blood pressure and apathy coincide in older persons with poorer functional ability: the Discontinuation of Antihypertensive Treatment in Elderly People (DANTE) Study Leiden. *J Am Geriatr Soc*. 2015; 63(1):112–117. [PubMed: 25597563]
18. Musini VM, Tejani AM, Bassett K, Wright JM. Pharmacotherapy for hypertension in the elderly. *Cochrane Database Syst Rev*. 2009; (4):CD00028.
19. Warwick J, Falaschetti E, Rockwood K, et al. No evidence that frailty modifies the positive impact of antihypertensive treatment in very elderly people: an investigation of the impact of frailty upon treatment effect in the HYpertension in the Very Elderly Trial (HYVET) study, a double-blind, placebo-controlled study of antihypertensives in people with hypertension aged 80 and over. *BMC Med*. 2015; 13:78. [PubMed: 25880068]
20. Group SR. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. *N Engl J Med*. 2015; 373(22):2103–2116. [PubMed: 26551272]
21. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J*. 2013; 34(28):2159–2219. [PubMed: 23771844]
22. James PAOS, Carter BL. Evidence-based guideline for the management of high blood pressure in adults report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014; 311(5):507–520. [PubMed: 24352797]
23. Muller M, Smulders YM, de Leeuw PW, Stehouwer CDA. Treatment of hypertension in the oldest old a critical role for frailty? *Hypertens*. 2014; 63(3):433–441.
24. Goodwin JS. Embracing complexity: a consideration of hypertension in the very old. *J Gerontol A Biol Sci Med Sci*. 2003; 58(7):M653–M658.
25. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged 75 years: a randomized clinical trial. *JAMA*. 2016
26. Odden MC, Peralta CA, Haan MN, Covinsky KE. Rethinking the association of high blood pressure with mortality in elderly adults: the impact of frailty. *Arch Intern Med*. 2012; 172(15):1162–1168. [PubMed: 22801930]
27. Odden MC, Covinsky KE, Neuhaus JM, Mayeda ER, Peralta CA, Haan MN. The association of blood pressure and mortality differs by self-reported walking speed in older Latinos. *J Gerontol A Biol Sci Med Sci*. 2012; 67(9):977–983. [PubMed: 22389463]

28. Cesari M, Fielding RA, Pahor M, et al. Biomarkers of sarcopenia in clinical trials—recommendations from the International Working Group on Sarcopenia. *J Cachexia, Sarcopenia Muscle*. 2012; 3(3):181–190. [PubMed: 22865205]
29. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001; 56(3):M146–M157. [PubMed: 11253156]
30. Taekema DG, Gussekloo J, Maier AB, Westendorp RG, de Craen AJ. Handgrip strength as a predictor of functional, psychological and social health. A prospective population-based study among the oldest old. *Age Ageing*. 2010; 39(3):331–337. [PubMed: 20219767]
31. Rantanen T, Guralnik JM, Foley D, et al. Midlife hand grip strength as a predictor of old age disability. *JAMA*. 1999; 281(6):558–560. [PubMed: 10022113]
32. Al Snih S, Markides KS, Ray L, Ostir GV, Goodwin JS. Handgrip strength and mortality in older Mexican Americans. *J Am Geriatr Soc*. 2002; 50(7):1250–1256. [PubMed: 12133020]
33. Gutiérrez-Misis A, Sánchez-Santos M, Banegas J, Castell M, González-Montalvo J, Otero A. Walking speed and high blood pressure mortality risk in a spanish elderly population. *J Hum Hypertens*. 2015; 29:566–572. [PubMed: 25880596]
34. Peralta CA, Katz R, Newman AB, Psaty BM, Odden MC. Systolic and diastolic blood pressure, incident cardiovascular events, and death in elderly persons: the role of functional limitation in the Cardiovascular Health Study. *Hypertension*. 2014; 64(3):472–480. [PubMed: 24935945]
35. Post Hoppers G, Smulders YM, Maier AB, Deeg DJ, Muller M. Relation between blood pressure and mortality risk in an older population: role of chronological and biological age. *J Intern Med*. 2015; 277(4):488–497. [PubMed: 25041041]
36. Sabayan B, van Vliet P, de Ruijter W, Gussekloo J, de Craen AJM, Westendorp RGJ. High Blood Pressure, Physical and Cognitive Function, and Risk of Stroke in the Oldest Old The Leiden 85-Plus Study. *Stroke*. 2013; 44(1):15–20. [PubMed: 23132780]
37. van Hateren KJJ, Hendriks SH, Groenier KH, et al. Frailty and the relationship between blood pressure and mortality in elderly patients with type 2 diabetes (Zwolle Outpatient Diabetes project Integrating Available Care-34). *J Hypertens*. 2015; 33(6):1162–1166. [PubMed: 25923730]
38. Weidung B, Boström G, Toots A, et al. Blood pressure, gait speed, and mortality in very old individuals: a population-based cohort study. *Journal Am Med Dir Assoc*. 2015; 16(3):208–214. [PubMed: 25441098]
39. Heeringa SG, Connor JH. Technical description of the health and retirement survey sample design. Ann Arbor: University of Michigan. 1995
40. Crimmins E, Guyer H, Langa K, Ofstedal MB, Wallace R, Weir D. Documentation of physical measures, anthropometrics and blood pressure in the Health and Retirement Study. HRS Documentation Report DR-011. 2008; 14:47–59.
41. Alley DE, Shardell MD, Peters KW, et al. Grip strength cutpoints for the identification of clinically relevant weakness. *J Gerontol A Biol Sci Med Sci*. 2014; 69(5):559–566. [PubMed: 24737558]
42. Cox DR. Regression models and life-tables. *J R Stat Soc B*. 1972:187–220.
43. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP; 2013. [computer program]
44. Peel NM, Kuys SS, Klein K. Gait speed as a measure in geriatric assessment in clinical settings: a systematic review. *J Gerontol A Biol Sci Med Sci*. 2013; 68(1):39–46. [PubMed: 22923430]
45. Van Kan GA, Rolland Y, Andrieu S, et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. *J Nutr Health Aging*. 2009; 13(10):881–889. [PubMed: 19924348]
46. Graham JE, Ostir GV, Kuo Y-F, Fisher SR, Ottenbacher KJ. Relationship between test methodology and mean velocity in timed walk tests: a review. *Arch Phys Med Rehabil*. 2008; 89(5):865–872. [PubMed: 18452733]
47. Leidy NK. Functional status and the forward progress of merry-go-rounds: toward a coherent analytical framework. *Nurs Res*. 1994; 43(4):196–202. [PubMed: 8047422]
48. Dorresteijn JA, van der Graaf Y, Spiering W, Grobbee DE, Bots ML, Visseren FL. Relation Between Blood Pressure and Vascular Events and Mortality in Patients With Manifest Vascular Disease J-Curve Revisited. *Hypertension*. 2012; 59(1):14–21. [PubMed: 22068865]

49. Bress AP, Tanner RM, Hess R, Colantonio LD, Shimbo D, Muntner P. Generalizability of results from the Systolic Blood Pressure Intervention Trial (SPRINT) to the US adult population. *J Am Coll Cardiol*. 2016; 67(5):463–472. [PubMed: 26562046]
50. Jochemsen HM, Muller M, Visseren FL, et al. Blood pressure and progression of brain atrophy: the SMART-MR Study. *JAMA Neurol*. 2013; 70(8):1046–1053. [PubMed: 23753860]
51. Muller M, Jochemsen H, Visseren F, et al. Low blood pressure and antihypertensive treatment are independently associated with physical and mental health status in patients with arterial disease: the SMART study. *JAMA Intern Med*. 2013; 274(3):241–251.

Figure 1.

Association of Blood Pressure with Death by the Combination of Grip Strength and Gait Speed (participants who died within the first two years of follow-up were excluded).

Footnote: Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure.

Weak grip strength: < 16 kg for female and < 26 kg for male.

Slow walkers: gait speed < 0.52 m/s for female and < 0.60 m/s for male.

Table 1

Characteristics of Adults Aged at Least 65 Years across Grip Strength

	Weak ^a (n = 1077)	Normal ^b (n = 6415)	P Value ^c
Age, mean (SD), y	79.5 (7.6)	73.5 (6.3)	<.001
Male, No. (%)	395 (36.7)	2876 (44.8)	<.001
White (vs. others), No. (%)	951 (88.3)	5494 (85.6)	.02
Education, mean (SD), y	12.0 (3.3)	12.4 (3.1)	<.001
< High school, No. (%)	306 (28.4)	1505 (23.5)	
= High school, No. (%)	380 (35.3)	2299 (35.9)	
> High school, No. (%)	391 (36.3)	2609 (40.7)	
Smoking status, No. (%)			.002
Never	497 (46.2)	2713 (42.3)	
Former	496 (46.1)	3053 (47.6)	
Current	72 (6.7)	617 (9.6)	
Cardiac disease, No. (%)	433 (40.2)	1882 (29.4)	<.001
Stroke, No. (%)	142 (13.2)	422 (6.6)	<.001
Diabetes, No. (%)	250 (23.2)	1358 (21.2)	.13
Cancer, No. (%)	229 (21.3)	1200 (18.7)	.05
Lung disease, No. (%)	153 (14.2)	694 (10.8)	.001
Arthritis, No. (%)	828 (77.0)	4302 (67.1)	<.001
Antihypertensives, No. (%)	676 (62.8)	3767 (58.7)	.01
SBP, mean (SD), mmHg	133.3 (22.0)	134.5 (20.6)	.08
DBP, mean (SD), mmHg	76.1 (12.1)	76.8 (11.4)	<.001
BMI, mean (SD), kg/m ²	25.9 (5.3)	27.6 (5.1)	<.001
Total cholesterol, mean (SD), mg/dL	197.2 (57.5)	202.4 (55.7)	.01
HDL cholesterol, mean (SD), mg/dL	59.1 (18.3)	59.8 (19.7)	.31
HbA1c, mean (SD), %	5.8 (0.8)	5.8 (0.8)	.78
Cystatin C, mean (SD), mg/L	0.8 (0.5)	0.7 (0.3)	<.001
C reactive protein, mean (SD), μg/L	2.5 (5.3)	2.1 (4.0)	.07

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; HDL, high density lipoprotein; HbA1c, glycosylated hemoglobin.

^aGrip strength <26 kg for male and <16 kg for female.

^bGrip strength ≥26 kg for male and ≥16 kg for female.

^cP values from two-sample t-tests for continuous variables and χ^2 tests for categorical variables.

Table 2

Association of Blood Pressure with Mortality by Grip Strength

	Weak ^a (n = 1077)	Normal ^b (n = 6415)	P for interaction
Systolic Blood Pressure			
Death rate per 1000 PYs			
150 mmHg	92.8	47.0	
< 150 mmHg	83.5	32.3	
Rate difference	9.3	14.7	
150 vs. <150 mmHg			
Unadjusted HR (95% CI)	1.12 (0.90, 1.38)	1.47 (1.31, 1.65) ***	.03
Adjusted HR (95% CI) ^c	0.94 (0.69, 1.27)	1.24 (1.07, 1.43) **	.07
Per 10 mmHg higher			
Unadjusted HR (95% CI)	1.00 (0.96, 1.05)	1.06 (1.04, 1.09) ***	.03
Adjusted HR (95% CI) ^c	0.97 (0.91, 1.02)	1.02 (0.99, 1.06)	.07
Diastolic Blood Pressure			
Death rate per 1000 PYs			
90 mmHg	76.8	37.4	
< 90 mmHg	86.6	35.0	
Rate difference	-9.8	2.4	
90 vs. <90 mmHg			
Unadjusted HR (95% CI)	0.89 (0.66, 1.18)	1.07 (0.93, 1.22)	.26
Adjusted HR (95% CI) ^c	0.84 (0.56, 1.26)	1.25 (1.05, 1.49) *	.07
Per 10 mmHg higher			
Unadjusted HR (95% CI)	0.91 (0.84, 0.99) *	0.93 (0.89, 0.98) **	.09
Adjusted HR (95% CI) ^c	0.95 (0.86, 1.05)	1.05 (0.99, 1.12)	.58

Abbreviations: PYs, person-years; HR, hazard ratio; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure.

^aGrip strength <26 kg for male and <16 kg for female.

^bGrip strength ≥26 kg for male and ≥16 kg for female.

^cAdjusted for age, sex, race (white, non-white), years of education, smoking status (current, former, never), body mass index, antihypertensive medication, stroke, cardiac disease, cancer, diabetes, high-density lipoprotein cholesterol, total cholesterol, cystatin C, glycosylated hemoglobin, and C reactive protein.

* $P < 0.05$,

** $P < 0.01$,

*** $P < 0.001$

Table 3

Association of Blood Pressure with Mortality by the Combination of Grip Strength and Gait Speed

	Slow walkers ^a with weak grip strength ^b n = 458	Slow walkers ^a with normal grip strength ^b or non-slow walkers ^c with weak grip strength ^d n = 1659	Non-slow walkers ^c with normal grip strength ^d n = 5375
Systolic blood pressure			
Death rate per 1000 PYs			
150 mmHg	118.3	78.8	40.4
< 150 mmHg	131.1	62.6	26.7
Rate difference	-12.8	16.2	13.7
150 vs. <150 mmHg			
Unadjusted HR (95% CI)	0.90 (0.68, 1.19)	1.26 (1.05, 1.51) ***	1.53 (1.33, 1.76) ***
Adjusted ^e HR (95% CI) ^f	0.85 (0.56, 1.29)	1.16 (0.91, 1.48)	1.24 (1.04, 1.47) ***
Diastolic blood pressure			
Death rate per 1000 PYs			
90 mmHg	89.0	75.5	30.7
< 90 mmHg	135.3	64.5	29.3
Rate difference	-46.3	11.0	1.4
90 vs. <90 mmHg			
Unadjusted HR (95% CI)	0.65 (0.44, 0.96) *	1.17 (0.94, 1.45)	1.05 (0.89, 1.23)
Adjusted ^e HR (95% CI) ^g	0.53 (0.30, 0.96) *	1.50 (1.13, 1.98) **	1.15 (0.94, 1.41)

Abbreviations: PYs, person-years; HR, hazard ratio; CI, confidence interval.

^aSlow walkers: gait speed <0.52 m/s for female and <0.60 m/s for male.^bWeak grip strength: <16 kg for female and <26 kg for male.^cNon-slow walkers: gait speed ≥ 0.52 m/s for female and ≥ 0.60 m/s for male.^dNormal grip strength: ≥ 16 kg for female and ≥ 26 kg for male.^eAdjusted for age, sex, race (white, non-white), years of education, smoking status (current, former, never), body mass index, antihypertensive medication, stroke, cardiac disease, cancer, diabetes, high-density lipoprotein cholesterol, total cholesterol, cystatin C, glycosylated hemoglobin, and C reactive protein.^fP for global test of the interaction term < .001^gP for global test of the interaction term < .001

* P < 0.05,

** P < 0.01,

*** P < 0.001

Table 4

Association of Blood Pressure with Mortality across Grip Strength and Gait Speed (participants who died within the first two years of follow-up were excluded).

		Grip Strength		P for interaction
		Weak ^a (n = 935)	Normal ^b (n = 6144)	
		HR (95% CI)		
SBP	150 vs. <150 mmHg			
	Unadjusted	1.00 (0.83, 1.20)	1.32 (1.18, 1.46) ***	.01
	Adjusted ^c	0.87 (0.67, 1.12)	1.13 (0.99, 1.29)	.06
DBP	90 vs. <90 mmHg			
	Unadjusted	0.79 (0.56, 1.12)	1.11 (0.96, 1.29)	.07
	Adjusted ^c	0.64 (0.39, 1.03)	1.27 (1.06, 1.53) **	.01

Abbreviations: HR, hazard ratio; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure.

^a Grip strength <16 kg for female and <26 kg for male.

^b Grip strength 16 kg for female and 26 kg for male.

^c Adjusted for age, sex, race (white, non-white), years of education, smoking status (current, former, never), body mass index, antihypertensive medication, stroke, cardiac disease, cancer, diabetes, high-density lipoprotein cholesterol, total cholesterol, cystatin C, glycosylated hemoglobin, and C reactive protein.

* $P < 0.05$,

** $P < 0.01$,

*** $P < 0.001$