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Effect of Intensive Blood Pressure Control on Gait Speed and Mobility Limitation in Adults 75 Years or Older
A Randomized Clinical Trial

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IMPORTANCE Intensive blood pressure (BP) control confers a benefit on cardiovascular morbidity and mortality; whether it affects physical function outcomes is unknown.

OBJECTIVE To examine the effect of intensive BP control on changes in gait speed and mobility status.

DESIGN, SETTING, AND PARTICIPANTS This randomized, clinical trial included 2636 individuals 75 years or older with hypertension and no history of type 2 diabetes or stroke who participated in the Systolic Blood Pressure Intervention Trial (SPRINT). Data were collected from November 8, 2010, to December 1, 2015. Analysis was based on intention to treat.

INTERVENTIONS Participants were randomized to intensive treatment with a systolic BP target of less than 120 mm Hg (n = 1317) vs standard treatment with a BP target of less than 140 mm Hg (n = 1319).

MAIN OUTCOMES AND MEASURES Gait speed was measured using a 4-m walk test. Self-reported information concerning mobility was obtained from items on the Veterans RAND 12-Item Health Survey and the EQ-5D. Mobility limitation was defined as a gait speed less than 0.6 meters per second (m/s) or self-reported limitations in walking and climbing stairs.

RESULTS Among the 2629 participants in whom mobility status could be defined (996 women [37.9%]; 1633 men [62.1%]; mean [SD] age, 79.9 [4.0] years), median [interquartile range] follow-up was 3 (2-3) years. No difference in mean gait speed decline was noted between the intensive- and standard-treatment groups (mean difference, 0.0004 m/s per year; 95% CI, −0.005 to 0.005; P = .88). No evidence of any treatment group differences in subgroups defined by age, sex, race or ethnicity, baseline systolic BP, chronic kidney disease, or a history of cardiovascular disease were found. A modest interaction was found for the Veterans RAND 12-Item Health Survey Physical Component Summary score, although the effect did not reach statistical significance in either subgroup, with mean differences of 0.004 (95% CI, −0.002 to 0.010) m/s per year among those with scores of at least 40 and −0.008 (95% CI, −0.016 to 0.001) m/s per year among those with scores less than 40 (P = .03 for interaction). Multistate models allowing for the competing risk of death demonstrated no effect of intensive treatment on transitions to mobility limitation (hazard ratio, 1.06; 95% CI, 0.92-1.22).

CONCLUSIONS AND RELEVANCE Among adults 75 years or older in SPRINT, treating to a systolic BP target of less than 120 mm Hg compared with a target of less than 140 mm Hg had no effect on changes in gait speed and was not associated with changes in mobility limitation.

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Supplemental content

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Results from the Systolic Blood Pressure Intervention Trial (SPRINT) indicate that targeting a systolic blood pressure (BP) of less than 120 mm Hg confers benefits on cardiovascular morbidity and mortality in adults 50 years or older with hypertension and free of type 2 diabetes and stroke.[1] This benefit was apparent in adults 75 years or older and, in exploratory analyses, among persons with frailty or slow gait speed.[2] A critical direction for SPRINT is to evaluate the balance between this benefit and other health consequences of intensive BP control.[3] This direction is especially true for adults 75 years or older, among whom 5.8 million individuals have been estimated to meet the SPRINT eligibility criteria.[4] Physical functioning during the course of the trial has yet to be reported.

Gait speed is a well-established physical function measure predictive of adverse health outcomes and mortality.[5,6] Decline in gait speed may be an early harbinger of decline in physical function, the development of disability, and loss of independence.[7] Observational evidence suggests a faster rate of gait speed decline among older adults with high BP.[8] In contrast, some evidence suggests that among very old adults, lower systolic BP is associated with greater limitations on activities of daily living and greater probability of worsening disability.[9] To our knowledge, no large-scale randomized clinical trials of BP control have reported on gait speed as an outcome.

Herein we compare the trajectory of gait speed decline and incident mobility limitation in the intensive- and standard-treatment groups in SPRINT within the subgroup of participants 75 years or older at the time of randomization. The findings of this study will help inform our understanding of the effect of intensive BP control on the net balance of health outcomes in older adults with hypertension.

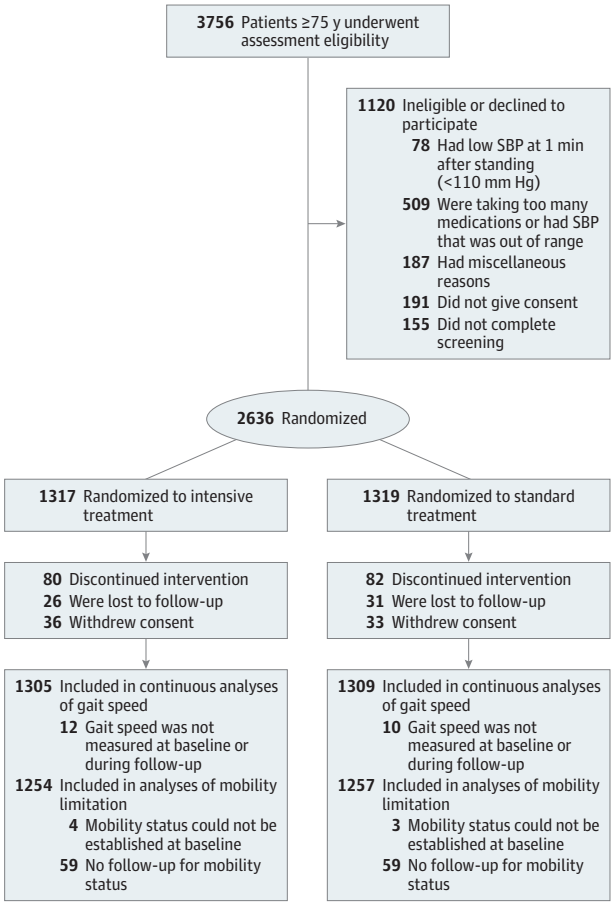
Key Points

Question Does targeting a systolic blood pressure of less than 120 mm Hg affect gait speed among adults 75 years or older with hypertension?

Findings In this randomized clinical trial of 2636 individuals, no differences were found between the intensive- and standard-treatment groups on changes in gait speed or mobility limitation during 3 years of follow-up.

Meaning Intensive blood pressure control does not appear to have an important effect on short-term gait speed decline among older adults.

Figure 1. CONSORT Diagram for the Systolic Blood Pressure Intervention Trial (SPRINT)



SBP indicates systolic blood pressure. Standard treatment indicates a blood pressure target of less than 140 mm Hg; intensive treatment, less than 120 mm Hg.

Methods

Population

The design, eligibility, and baseline characteristics of SPRINT have been described previously,[10] and a copy of the study protocol is available in Supplement 2. The CONSORT diagram for the study is shown in **Figure 1**. Of 9361 participants randomized to an intensive systolic BP target of less than 120 mm Hg or a standard target of less than 140 mm Hg, 2636 were 75 years or older. The characteristics of participants in this subgroup by treatment group have been previously described.[2] The only statistically significant treatment group differences at baseline were a higher frequency of aspirin use (820 [62.3%] vs 765 [58.0%]) and higher prevalence of frailty, as assessed by a 37-item frailty index[11] (440 [33.4%] vs 375 [28.4%]) in the intensive-treatment group. This study was approved by the institutional review board at each participating site, and all patients provided written informed consent.

Study Measurements

Demographic, clinical, and laboratory data were collected at baseline. Race or ethnicity data were collected by self-report. Body mass index was calculated as weight in kilograms divided by the square of the height in meters. The estimated glomerular filtration rate (eGFR) was calculated by the 4-variable Modification of Diet in Renal Disease study equation.[12] Physical and mental health-related quality of life were assessed using the Veterans RAND 12-Item Health Survey (VR-12).[13] The VR-12 is summarized via the Physical Component Summary (PCS) and Mental Component Summary scores;

for each component, a score of 50 represents the US population mean; 10 points represent 1 SD; and higher scores denote better quality of life (QOL).[14]

Gait Speed Measurements

Gait speed was measured at the time of randomization and annually thereafter via a timed 4-m walk performed twice at the participant's usual pace from a standing start. The use of a walking assistive device was permitted if typically used by the participant to walk short distances. The faster of the 2 gait speeds in meters per second was used in this analysis. Gait speeds slower than 0.20 meters per second (m/s) and faster than 2.0 m/s (to convert to miles per hour, multiply by 2.237) were set to missing (n = 22).

Self-reported Mobility

We considered 2 self-reported questions concerning mobility from QOL instruments administered at baseline and then annually thereafter. From the VR-12,[13] we considered the question, "Does your health now limit you in climbing several flights of stairs?" with responses of "yes, limited a lot," "yes, limited a little," or "no, not limited at all." We also considered the mobility question from the EQ-5D,[15] with responses of "I have no problems in walking about," "I have some problems in walking about," or "I am confined to bed." Mobility limitation was defined as (1) having a gait speed of less than 0.6 m/s[16] or (2) reporting a lot of difficulty climbing stairs and (3) reporting some difficulty walking about or being confined to bed (1 or both 2 and 3). As a secondary approach, we examined models that defined mobility limitation based solely on gait speed (<0.6 m/s). Because gait speed based on a 4-m walk test entails measurement error, we required that any changes in gait speed were at least 0.127 m/s (the 95% confidence limit for an estimated minimal detectable change[17]) to define a transition between mobility status for models defining mobility limitation based solely on gait speed. For example, if a participant's gait speed at baseline was 0.650 m/s, their gait speed would need to decrease to less than 0.523 m/s at a subsequent visit to be classified as having developed a mobility limitation.

Duration of Follow-Up

Recruitment for SPRINT began on November 8, 2010. The director of the National Heart, Lung, and Blood Institute accepted the Data Safety and Monitoring Board recommendation to stop the SPRINT intervention on August 20, 2015. To maximize the number of follow-up assessments for gait speed, we included study visits through December 1, 2015. Our analysis includes 527 gait speed assessments during a period where participants were transitioning to having their BP managed by their primary care physician. When we compared BPs in the 103-day period from August 20 to December 1, 2015, with BPs measured in the 103 days before August 20, 2015, the mean systolic BP increased slightly in both treatment groups, from 133.6 to 135.5 mm Hg in the standard-treatment group and from 118.4 to 121.3 mm Hg in the intensive-treatment group. However, the mean systolic BP difference decreased by only approximately 1 mm Hg during this transition period, from 15.2 (95% CI, 14.6 to 15.8) mm Hg to 14.1 (95% CI, 13.5 to 14.7) mm Hg.

Statistical Analysis

Analysis was based on intention to treat. We used linear mixed-effect models, assuming linear decline, to compare longitudinal trajectories for gait speed between the treatment groups. The models included nested random effects (participants within clinic site) to address within-participant correlations owing to repeated assessments and correlations between participants at the same clinical site. We included a time by randomization group interaction term to test whether the change in gait speed differed between the treatment groups. The mixed models were fit using SAS software (version 9.4; SAS Institute Inc). We tested for interaction between treatment group and the following subgroups: age (<80 vs ≥80 years), sex, race (black vs nonblack), baseline systolic BP (<140, 140-159, or ≥160 mm Hg), presence of chronic kidney disease (eGFR <60 mL/min/1.73 m^2), history of cardiovascular disease (CVD), and VR-12 PCS score (≥40 vs <40).

Sensitivity Analyses

We conducted 2 sensitivity analyses for the models of change in gait speed. We used multiple imputation techniques to infer missing gait speed measurements, using the same mixed-effect model framework described above. Details about the multiple imputation procedure are described in the eMethods in Supplement 1. Next, we censored gait speed measures at the time of the National Heart, Lung, and Blood Institute director's decision to stop the SPRINT intervention.

Multistate Modeling

We examined transitions in mobility status using a multistate model as shown in the eFigure in Supplement 1; this method accounts for the competing risk of death. Mobility limitation was defined based on gait speed and self-reported limitation in walking and climbing stairs, as described above. The model included the following 3 states: alive with no mobility limitation, alive with a mobility limitation, and death. We conducted a secondary analysis of mobility limitation defined by gait speed alone as described above. The multistate models were fit using the mstate package for the R statistical computing environment.[18,19]

Results

Among 2636 randomized participants 75 years or older, 2629 (99.7%) had information on mobility at baseline (996 women [37.9%] and 1633 men [62.1%]; mean [SD] age, 79.9 [4.0] years) (**Table 1** and eTable 1 in Supplement 1). In defining mobility status at baseline, 2541 participants had gait speed measured, whereas mobility status was based solely on self-report in an additional 88 participants. Of these, 464 (17.6%) were classified as having a mobility limitation at baseline, with similar frequencies in the intensive-treatment (233 of 1313 [17.7%]) and standard-treatment (231 of 1316 [17.6%]) groups. Participants with a mobility limitation were older and more likely to be female and not white. They had a higher body mass index and albumin to creatinine ratio and lower eGFR than participants without a mobility limitation.

Table 1. Baseline Characteristics of SPRINT Participants 75 Years or Older by Mobility Status

Characteristic	Mobility Group, No. (%)[a]		P Value
	No Mobility Limitation (n = 2165)	Mobility Limitation (n = 464)	
Randomized to intensive treatment, (%)[b]	1080 (49.9)	233 (50.2)	.94
Age, mean (SD), y	79.6 (3.8)	81.0 (4.6)	<.001
Age ≥80 y	909 (42.0)	254 (54.7)	<.001
Females	770 (35.6)	226 (48.7)	<.001
Race or ethnicity			
White	1676 (77.4)	284 (61.2)	<.001
Black	330 (15.2)	120 (25.9)	
Hispanic	115 (5.3)	57 (12.3)	
Other	44 (2.0)	3 (0.6)	
SBP, mean (SD), mm Hg	141.5 (15.8)	142.5 (15.7)	.19
SBP			.77
<140 mm Hg	1024 (47.3)	211 (45.5)	
140-159 mm Hg	868 (40.1)	192 (41.4)	
≥160 mm Hg	273 (12.6)	61 (13.1)	
Diastolic BP, mean (SD), mm Hg	71.3 (10.9)	70.7 (11.0)	.25
BMI, mean (SD)	27.5 (4.4)	29.0 (5.8)	<.001
Serum creatinine level, median (IQR), mg/dL	1.1 (0.9-1.3)	1.1 (0.9-1.3)	.11
eGFR, mean (SD), mL/min/1.73 m^2[c]	63.8 (17.7)	61.4 (20.2)	.01
eGFR<60 mL/min/1.73 m^2[c,d]	927 (43.0)	233 (50.7)	.003
Urine albumin to creatinine ratio, median (IQR), mg/g	12.4 (7.0-29.8)	16.9 (9.6-40.3)	<.001
History of cardiovascular disease	525 (24.2)	121 (26.1)	.44
No. of antihypertensives used at baseline, mean (SD)	1.9 (1.0)	2.1 (1.0)	<.001
Statin use at baseline[d]	1143 (53.2)	235 (51.3)	.49
Aspirin use at baseline[d]	1326 (61.4)	259 (55.9)	.04
10-y Framingham CVD Risk Score, median (IQR), %[e]	24.8 (17.0-33.0)	23.6 (16.2-33.3)	.34
VR-12 PCS score, mean (SD)[f]	46.2 (8.5)	34.1 (10.6)	<.001
VR-12 MCS score, mean (SD)[f]	55.4 (8.0)	53.7 (10.0)	<.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BP, blood pressure; eGFR, estimated glomerular filtration rate; IQR, interquartile range; MCS, Mental Component Summary; PCS, Physical Component Summary; SBP, systolic BP; SPRINT, Systolic Blood Pressure Intervention Trial; VR-12, Veterans RAND 12-Item Health Survey.

SI conversion factor: To convert creatinine to micromoles per liter, multiply by 88.4.

[a] Mobility limitation was defined as (1) having a gait speed of less than 0.6 meters per second (m/s) or (2) reporting a lot of difficulty climbing stairs and (3) reporting some difficulty walking about or being confined to bed. Percentages have been rounded and may not total 100.

[b] Indicates a BP target of less than 120 mm Hg.

[c] Based on the Modification of Diet in Renal Disease study equation.

[d] A small number of data were missing; therefore, denominators may not be the total in the column head.

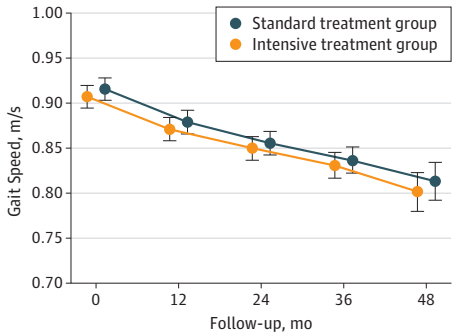
[e] Higher values indicate higher predicted probability of cardiovascular disease across 10 years.[20]

[f] A score of 50 represents the US population mean; 10 points represent 1 SD; and higher scores denote better quality of life.[14]

Participants with a mobility limitation used more antihypertensives and were more likely to use aspirin at baseline. No difference was found between groups in history of CVD or in Framingham CVD risk score[20] (Table 1).

The mean gait speed at baseline was 0.91 m/s, with a mean annual change of −0.026 (95% CI, −0.028 to −0.023) m/s. The trajectory of gait speed appeared similar among participants in the intensive- and standard-treatment groups (**Figure 2**). We found no difference in mean gait speed decline between participants randomized to intensive treatment and those randomized to standard treatment (mean difference, 0.0004 m/s per year; 95% CI, −0.005 to 0.005 m/s per year; P = .88 for difference) (**Table 2**). The change in gait speed between the intensive- and standard-treatment groups did not differ significantly for subgroups defined by age, sex, race or ethnicity, baseline systolic BP, chronic kidney disease, or history of CVD (Table 2). The effect of intensive treatment on change in gait speed was modestly more beneficial among those with higher VR-12 PCS scores, although the effect on change in gait speed did not reach statistical significance in either group, with mean differences of 0.004 (95% CI, −0.002 to 0.010) m/s among those with PCS scores of at least 40 and −0.008 (95% CI, −0.016 to 0.001) m/s among those with PCS scores less than 40 (P = .03).

Figure 2. Least Squares Means for Gait Speed by Treatment Group During the Course of Follow-up



No. at risk

Standard treatment group	1272	1150	1086	790	265
Intensive treatment group	1269	1160	1101	822	252

Circles denote estimated least squares mean for gait speed based on linear mixed model, treating time discretely (0, 12, 24, 36, and 48 months). Error bars represent 95% CIs. Standard treatment indicates a blood pressure target of less than 140 mm Hg; intensive treatment, less than 120 mm Hg.

The proportion of missing data for gait speed appeared similar between the intensive- and standard-treatment groups and

Table 2. Linear Mixed-Effect Model Estimates of Annual Change in Gait Speed by Treatment Group and for Subgroups[a]

Subgroup	No. of Participants[b]	Annual Change in Gait Speed (95% CI), m/s		Difference (95% CI), m/s	*P* Value	*P* Value for Interaction
		Intensive-Treatment Group	Standard-Treatment Group			
Overall	2614	−0.026 (−0.029 to −0.022)	−0.026 (−0.029 to −0.022)	0.0004 (−0.005 to 0.005)	.88	
Age, y						
<80	1461	−0.023 (−0.028 to −0.019)	−0.021 (−0.026 to −0.017)	−0.002 (−0.008 to 0.005)	.57	.29
≥80	1153	−0.029 (−0.035 to −0.024)	−0.033 (−0.038 to −0.028)	0.004 (−0.004 to 0.011)	.36	
Sex						
Males	1627	−0.025 (−0.029 to −0.020)	−0.028 (−0.032 to −0.023)	0.003 (−0.004 to 0.009)	.37	.21
Females	987	−0.027 (−0.032 to −0.021)	−0.023 (−0.028 to −0.018)	−0.004 (−0.011 to 0.004)	.36	
Race or ethnicity						
Nonblack	2153	−0.027 (−0.030 to −0.023)	−0.027 (−0.031 to −0.023)	0.0005 (−0.005 to 0.006)	.87	.91
Black	461	−0.021 (−0.029 to −0.013)	−0.021 (−0.029 to −0.012)	−0.0003 (−0.012 to 0.011)	.96	
SBP, mm Hg						
<140	1227	−0.024 (−0.029 to −0.013)	−0.024 (−0.029 to −0.019)	−0.0001 (−0.007 to 0.007)	.97	.44
140-159	1056	−0.025 (−0.031 to −0.019)	−0.028 (−0.034 to −0.023)	0.003 (−0.005 to 0.011)	.44	
≥160	331	−0.033 (−0.043 to −0.024)	−0.026 (−0.035 to −0.017)	−0.007 (−0.020 to 0.006)	.27	
Previous CKD						
No	1446	−0.023 (−0.027 to −0.018)	−0.025 (−0.030 to −0.020)	0.002 (−0.004 to 0.009)	.53	.52
Yes	1156	−0.029 (−0.034 to −0.024)	−0.028 (−0.033 to −0.023)	−0.001 (−0.009 to 0.006)	.77	
Previous CVD						
No	1972	−0.026 (−0.031 to −0.022)	−0.024 (−0.028 to −0.020)	−0.002 (−0.008 to 0.004)	.50	.09
Yes	642	−0.023 (−0.029 to −0.017)	−0.031 (−0.038 to −0.024)	0.008 (−0.001 to 0.017)	.09	
VR-12 PCS score[c]						
≥40	1769	−0.023 (−0.027 to −0.018)	−0.027 (−0.031 to −0.022)	0.004 (−0.002 to 0.010)	.17	.03
<40	835	−0.032 (−0.038 to −0.026)	−0.024 (−0.030 to −0.018)	−0.008 (−0.016 to 0.001)	.07	

Abbreviations: CKD, chronic kidney disease; CVD, cardiovascular disease; m/s, meters per second; PCS, Physical Component Summary; SBP, systolic blood pressure.

[a] For the treatment group differences, negative values indicate a faster rate of decline in gait speed for the intensive-treatment group. Standard treatment indicates a blood pressure target of less than 140 mm Hg; intensive treatment, less than 120 mm Hg.

[b] Denotes the number of participants with at least 1 assessment of gait speed (at baseline or during the course of follow-up).

[c] A score of 50 represents the US population mean; 10 points represent 1 SD; and higher scores denote better quality of life.[14]

ranged from less than 5% at baseline to approximately 20% at 36 and 48 months (eTable 1 in Supplement 1). The proportion of missing data over time was greater among those with a mobility limitation at baseline than those without a mobility limitation (eTable 2 in Supplement 1). Multiple imputation of missing gait speed measures did not alter the results. Assuming missingness at random, the difference in mean gait speed decline per year between the intensive- and standard-treatment groups was −0.00005 m/s (95% CI, −0.005 to 0.005 m/s; $P = .98$) after imputation. Censoring follow-up at the time of the decision to stop the SPRINT intervention also did not affect the results; the difference in mean gait speed decline per year was also −0.0002 m/s (95% CI, −0.006 to 0.005 m/s; $P = .93$ for difference).

The mean transition rate from no mobility limitation to mobility limitation was 12.5 per 100 person-years. Transitions from no mobility limitation to mobility limitation and vice versa did not differ in the intensive- and standard-treatment groups (**Table 3**). We found no effect of intensive treatment on transitions to mobility limitation (hazard ratio, 1.06; 95% CI, 0.91-1.22) or on transitions from mobility limitation to no mobility limitation (hazard ratio, 0.92; 95% CI, 0.77-1.10). Participants in the intensive-treatment group with no mobility limitation had a lower risk for death than those in the standard-treatment group (hazard ratio, 0.62; 95% CI, 0.43-0.90). Findings were unchanged when we restricted the definition of mobility limitation to consider only clinically relevant changes in gait speed, although the effect of intensive BP control on mortality (from a state of no mobility limitation) was no longer statistically significant.

Discussion

Among adults 75 years or older in SPRINT, we found no differences in gait speed decline among those in the intensive- vs standard-treatment groups. In both groups, the mean rate of gait speed decline was approximately 0.08 m/s across 3 years. In addition, intensive treatment was not associated with changes in mobility limitation compared with standard treatment. These findings were robust to statistical attempts to account for missing data and the competing risk for death. The effect of intensive lowering of BP on the change in gait speed was consistent across subgroups defined by age, sex, race, systolic BP, history of chronic kidney disease, and history of CVD, although we found modest evidence of a differential effect by physical QOL.

Table 3. Effect of Intensive vs Standard Treatment on Transition Probabilities for Multistate Model of Mobility Limitation Accounting for the Competing Risk of Death[a]

Model[b]	Intensive-Treatment Group		Standard-Treatment Group		Hazard Ratio (95% CI)	*P* Value
	No. of Observations[c]	Rate[d]	No. of Observations[c]	Rate[d]		
Based on gait speed and self-report, transition						
No mobility limitation → mobility limitation	366	12.83	357	12.20	1.06 (0.91-1.22)	.46
No mobility limitation → death	46	1.61	74	2.53	0.62 (0.43-0.90)	.01
Mobility limitation → no mobility limitation	238	32.04	238	34.66	0.92 (0.77-1.10)	.38
Mobility limitation → death	35	4.71	44	6.41	0.82 (0.52-1.28)	.38
Based on gait speed only, transition						
No mobility limitation → mobility limitation	176	5.86	170	5.49	1.09 (0.88-1.35)	.42
No mobility limitation → death	62	2.06	85	2.74	0.74 (0.54-1.04)	.08
Mobility limitation → no mobility limitation	82	22.93	80	26.39	0.86 (0.63-1.17)	.33
Mobility limitation → death	15	4.19	25	8.25	0.56 (0.29-1.07)	.08

[a] Standard treatment indicates a blood pressure target of less than 140 mm Hg; intensive treatment, less than 120 mm Hg.

[b] For gait speed and self-report model, mobility limitation was defined as (1) having a gait speed of less than 0.6 meters per second (m/s) or (2) reporting a lot of difficulty climbing stairs and (3) reporting some difficulty walking about being confined to bed. For the gait speed only model, mobility limitation was based solely on gait speed (<0.6 m/s), requiring that any changes in gait speed were at least 0.127 m/s to define a transition between the 2 mobility states (see Methods).

[c] Indicates number of times each transition was observed.

[d] Indicates rate of each transition per 100 person-years of follow-up.

SPRINT is, to our knowledge, the first large-scale randomized clinical trial of BP control to report results concerning gait speed as an outcome. Our findings are consistent with findings from the Systolic Hypertension in the Elderly Program (SHEP),[21] which found no significant differences in change in function in basic, moderate, or advanced activities of daily living. However, a subsequent report[22] demonstrated that the presence of missing data may have biased the findings against a benefit of the treatment group. In addition, investigators from the SHEP trial[21] found a modest benefit of treatment on self-reported evening walks, considered a leisure time activity in the SHEP questionnaire. The ongoing Intensive vs Standard Ambulatory Blood Pressure Lowering to Prevent Functional Decline in the Elderly (INFINITY) trial[23] may provide additional insight regarding the role of ambulatory BP control on mobility outcomes.

Observational evidence of the effect of BP on gait speed is mixed, although most of it points toward an association of higher BP and worse gait function among older adults. In the Cardiovascular Health Study, participants with a BP of higher than 140/90 mm Hg had a faster rate of decline in gait speed than those without increased BP.[8] In the Lifestyle Interventions and Independence for Elders Pilot (LIFE-P) trial,[24] investigators found that wider pulse pressure was associated with slower gait. A small study of older adults found that adults with hypertension had worse gait function variables, although not slower gait speed.[25] Worsening gait and functional performance have been hypothesized to be due to increased white matter hyperintensities among individuals with hypertension. Investigators in the Health, Aging, and Body Composition (Health ABC) study[26] found that white matter hyperintensities among specific regions were associated with slower gait. However, some evidence suggests the opposite association may exist among very old individuals. Investigators from the Leiden-85 Plus study found that higher systolic BP was associated with less worsening of activities of daily living compared with lower BP.[9] However, limitations in activities of daily living are likely to be downstream of changes in mobility status, so these conflicting findings may be due to the evaluation of the role of BP at differing stages of the disablement process.

We found modest evidence of an interaction by physical QOL, such that among those with better physical QOL, intensive BP lowering appeared to be associated with a slower rate of decline in gait speed, whereas among those with worse physical QOL, intensive BP lowering appeared to be associated with a faster decline in gait speed. Participants with preserved physical QOL may have gained additional benefit from intensive treatment. However, these findings should be interpreted with caution because the effect size was modest and did not reach statistical significance in either group. Further research is needed to determine whether some factors can differentiate the populations for whom intensive BP treatment may slow or accelerate gait speed decline.

Several possible reasons explain why intensive treatment did not substantially affect gait speed or mobility outcomes in SPRINT participants 75 years or older or in most of the subgroups examined. Gait speed incorporates function across multiple domains, including cardiorespiratory fitness, musculoskeletal health, vision, balance, and even mood or psychosocial health[5,16]; therefore, the cardiovascular benefit conferred from intensive BP control might not extend to mobility outcomes owing to the multifactorial nature of mobility. The literature on heart failure presents a similar conundrum in that the optimal therapy can differ for the outcomes of survival and exercise capacity; medications that confer a survival benefit, such as β-adrenergic blockers, can negatively affect exercise capacity.[27,28] In addition, physical functioning is affected by a lifetime of exposures, so the intervention may not have been long enough to significantly affect mobility.

SPRINT participants 75 years or older had a mean decline in gait speed of approximately 0.08 m/s across the 3 years of follow-up. A pooled analysis of the association of gait speed

and survival found a 12% lower risk for mortality per 0.1-m/s increment of gait speed,[5] indicating that the change observed in SPRINT is clinically relevant. The gait speed decline observed in SPRINT is similar to that for other populations of older adults. In the Cardiovascular Health Study, a study of community-dwelling adults 65 years or older at baseline, gait speed declined a median of −0.2 m/s across 9 years,[29] or approximately 0.022 m/s per year. In the Health ABC study,[30] the estimated change in gait speed during 4 years was 0.10 m/s or a decline of 0.025 m/s per year. The mean annual decline in gait speed for participants aged 75 to 79 years in the Invecchiare in Chianti (InCHIANTI) study was 0.036 m/s per year for women and 0.034 m/s per year for men.[31]

Limitations

Our study has several limitations. SPRINT excluded individuals with a history of diabetes or stroke, symptomatic heart failure, or an indication for specific antihypertensives; thus, our findings may not be applicable to populations with these conditions. SPRINT also excluded individuals with orthostatic hypotension or dementia and did not enroll elderly persons living in nursing homes. Most SPRINT participants were already treated with antihypertensives; therefore, our results do not address the effect of initiating BP therapy. In addition, the clinic staff who performed gait speed assessments were not blinded to treatment assignment. A modest amount of data were missing, although this appeared evenly distributed across treatment groups and the results were unchanged when we used multiple imputation. Furthermore, the results were similar when we used gait speed alone as an outcome, or mobility limitation that included self-reported data. Finally, SPRINT was stopped early owing to a significantly lower rate of the primary composite outcome in the intensive-treatment group, so we are not able to look at the long-term effects of intensive BP lowering on gait and mobility outcomes. This early termination may have limited the trial's power to detect differences in gait speed or mobility limitation.

Conclusions

Intensive BP lowering was not associated with changes in gait speed or transitions in mobility status among adults 75 years or older in SPRINT. The benefits of intensive BP lowering on cardiovascular prevention and mortality do not appear to affect short-term mobility.

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Group Information: The members of the Systolic Blood Pressure Intervention Trial (SPRINT) Research Group are listed in the eAppendix in Supplement 1.

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