Blood Pressure and Lower Limb Function in Older Persons

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Background. Factors contributing to gait difficulties in elderly persons are considered to be multifactorial and are not well understood. The purpose of this study was to examine the association of blood pressure (BP) with change in lower limb function in older persons.

Methods. Eight hundred eighty-eight older Catholic clergy members without baseline dementia or Parkinson’s disease were recruited from about 40 groups across the United States. At baseline, BP was measured, the presence of vascular diseases and diabetes was recorded, cognitive function was assessed, and medications were inspected. At baseline and subsequent annual visits, gait and balance were assessed using performance-based tasks from which a previously established composite measure of lower limb function was derived.

Results. In a general estimating equation analysis controlling for age, education, and gender, a 10 mmHg increment in systolic blood pressure (SBP) was associated with greater decline in lower limb function (estimate of interaction $= -6.35 \times 10^{-3}$, standard error $= 2.49 \times 10^{-3}$, $p = .011$). Thus, on average, lower limb function declined 28.7% faster in persons with an SBP of 160 mmHg than in persons with an SBP of 120 mmHg. This effect was unchanged after controlling for baseline vascular diseases, diabetes, or cognition. However, censoring individuals who developed stroke during the study made the relationship between SBP and change in lower limb function nonsignificant.

Conclusions. SBP may be associated with decline in lower limb function in older persons.

Gait difficulties are common in older individuals (1) and are associated with dementia (2–4), disability (5–7), and mortality (8,9). Factors contributing to gait difficulties in elderly persons are not well understood. Clinical stroke (10) and white matter changes on neuroimaging (11,12) affect gait, and elevated blood pressure (BP) is associated with both conditions (13). Limited research on the relationship of BP and gait decline in older persons has been inconclusive, however (14).

The Religious Orders Study is an investigation of aging and Alzheimer’s disease in older Catholic clergy. At baseline, BP was measured, presence of vascular diseases and diabetes was determined, and cognition was assessed. At baseline and annual follow-up visits, lower limb function was assessed by using performance-based measures of gait and balance. Using general estimating equation analyses, we tested whether higher BP was related to decline in lower limb function.

METHODS

Participants

Older Catholic clergy from about 40 groups across the United States were recruited. All participants consented to annual clinical evaluations. The study was approved by the Rush Institutional Review Board.

From January 1994 through December 2005, 1058 persons completed the baseline clinical evaluation. Eighty-eight individuals were excluded because they died before their first follow-up, had not reached their first follow-up, had only one valid score for performance-based lower limb function, or had a missing baseline evaluation for Parkinson’s disease. Using previously described criteria (2,15,16), we excluded 8 individuals with Parkinson’s disease and 74 individuals with dementia at baseline. Analyses are based on the remaining 888 persons who completed an average of 7.8 (standard deviation [SD] = 3.2, range = 2–12) annual evaluations.

Assessment of Lower Limb Function

Two measures of gait speed, one measure of chair rise capacity, and two measures of balance skills were used to assess lower limb function at each evaluation, as previously described (17). The time and number of steps taken to walk 8 feet (2.4 m), the time to sit up and down five times, the number of steps off the line during an 8-foot heel-to-toe walk, and the total time able to maintain: (i) a full tandem stand with eyes open, (ii) a semitandem stand with eyes open, and (iii) a side-by-side stand with eyes open and with eyes closed were recorded. Each measure was scaled from 0 to 5, with 0 indicating inability to perform the task. For individuals able to perform the task, each distribution was divided into quintiles. A score of 5 was assigned to individuals in the best performance quintile and 1 to individuals in the worst performance quintile. We averaged these five moderately correlated (median $r = 0.39$) measures to create a composite measure of lower limb function, comparable to summary gait measures in other studies (18,19).
Effects of vascular disease, diabetes, and cognition on the relationship between BP and lower limb function were examined. First, stroke, myocardial infarction, and leg claudication and each variable’s interaction with time were added separately and then together into the basic model. Also, the basic model was repeated three times with censoring of individuals who developed stroke, myocardial infarction, or leg claudication, respectively. Next, we repeated the basic model by including a term for diabetes and its interaction with time. Finally, we repeated the basic model twice to censor individuals who developed incident dementia and to add baseline cognitive function and its interaction with time, respectively.

The relationship of alternate BP definitions with lower limb function was examined by replacing SBP with: (i) DBP; (ii) baseline use of medications with antihypertensive properties; (iii) SBP >160 mmHg; (iv) SBP >160 mmHg or use of medications with antihypertensive properties; (v) DBP >90 mmHg; or (vi) DBP >90 mmHg or use of medications with antihypertensive properties. Finally, linear and quadratic terms for SBP or DBP were used in models adjusted for age, education, and gender.

All models were validated graphically and analytically. Analyses were carried out in SAS (version 8; SAS Institute Inc., Cary, NC).

RESULTS

The mean age of participants was 75 years (SD = 7), their average education was 18 years (SD = 3), and 69% were women. With respect to baseline vascular disease, 6.2% had a stroke, 14.5% had a myocardial infarction, and 9.1% had leg claudication. Diabetes was present in 11.3% of the baseline population. The mean Mini-Mental Status Examination score was 28.5 (SD = 1.6). Of the participants, 49% were taking at least one medication with antihypertensive properties.

The mean baseline SBP was 135 mmHg (SD = 17, range = 90–209 mmHg), and the mean DBP was 75 mmHg (SD = 10, range = 20–119 mmHg). Age was positively correlated with SBP (r = 0.14, p < .001) but negatively correlated with DBP (r = −0.23, p < .001). Education was correlated with DBP (r = 0.11, p = .002) but not SBP (r = 0.01, p = .66). There was no gender difference in SBP [t(879) = 1.14, p = .255], but women had lower DBP than men [t(878) = −2.52, p = .012].

BP and Lower Limb Function

A generalized estimating equation model with terms for time, SBP, age, education, gender, and their interactions with time was constructed. As shown in Table 1, the average rate of decline in lower limb function was 9.79 × 10⁻² unit/year. A 10 mmHg increase in SBP was not associated with level of lower limb function, as shown by the main effect term for SBP. However, each 10 mmHg increase in SBP was associated with a 6.35 × 10⁻³ unit increase in rate of annual decline. As illustrated in Figure 1, lower limb function decline in persons with an SBP of 160 mmHg (92nd percentile) was about 28.7% faster than in persons with an SBP of 120 mmHg (18th percentile).

### Table 1. Relationship of Systolic Blood Pressure With Baseline Level of and Annual Rate of Change in Lower Limb Function*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Parameter Estimate</th>
<th>Standard Error</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>−9.79 × 10⁻²</td>
<td>4.57 × 10⁻³</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Systolic blood pressure³</td>
<td>−2.21 × 10⁻²</td>
<td>1.59 × 10⁻²</td>
<td>.165</td>
</tr>
<tr>
<td>Systolic blood pressure × Time³</td>
<td>−6.35 × 10⁻³</td>
<td>2.49 × 10⁻³</td>
<td>.011</td>
</tr>
</tbody>
</table>

Notes: *From generalized estimating equation model adjusted for age, education, and gender.
³Estimate represents the effect of a 10 mmHg difference in systolic blood pressure on annual change in lower limb function.
As BP is associated with cerebrovascular disease (25,26), we examined whether stroke mediated the relationship between SBP and lower limb function. When we added terms for baseline stroke and its interaction with time, SBP still was associated with decline in lower limb function. When we repeated the basic model censoring individuals who developed stroke during the study, the association of a 10 mmHg increment in SBP with decline in lower limb function was no longer significant (estimate of interaction $= -4.39 \times 10^{-3}, SE = 2.66 \times 10^{-3}, p = .099$).

Controlling for baseline myocardial infarction and leg claudication, respectively, did not alter the association of SBP with lower limb function decline. Censoring individuals with myocardial infarction resulted in a 10 mmHg increment in SBP with decline in lower limb function being associated with greater decline in lower limb function (estimate of interaction $= -9.40 \times 10^{-3}, SE = 2.94 \times 10^{-3}, p = .001$). However, censoring individuals with leg claudication did not alter the association of SBP and lower limb function decline (estimate of interaction $= -6.63 \times 10^{-3}, SE = 2.74 \times 10^{-3}, p = .001$). When all vascular disease terms were added in the basic model, a 10 mmHg increment in SBP still was associated with decline in lower limb function (estimate of interaction $= -6.68 \times 10^{-3}, SE = 2.73 \times 10^{-3}, p = .014$).

Whereas other analyses in the Religious Orders Study cohort have shown a relationship between diabetes and gait (27), diabetes did not alter the relationship between SBP and decline in lower limb function (results not shown). Gait difficulties also have been associated with dementia (2–4), and some studies have shown that high or low BP in late life is associated with dementia (28,29). When we censored individuals with incident dementia or added baseline cognitive function and its interaction with time, the association of SBP and lower limb function decline was not altered (results not shown).

Table 2 highlights the association of other BP representations and lower limb function. A 10 mmHg increment in DBP was not associated with baseline level of or change in lower limb function. Because Seeman and colleagues (14) found a marginal relationship between high BP (defined as a value $>140/90$ mmHg or antihypertensive medication use) and decline in gait, we examined the effects of use of antihypertensive medications and dichotomous BP variables (see Table 2). Use of medications with antihypertensive properties was not associated with lower limb function decline. SBP $>160$ mmHg was associated with decline in lower limb function; however, adding the use of medications with antihypertensive properties with SBP $>160$ mmHg was not associated with lower limb function decline. Similarly, DBP $>90$ mmHg was associated with change in lower limb function, whereas adding use of medications with antihypertensive properties to DBP $>90$ mmHg was not. When quadratic terms for SBP or DBP were used, a nonlinear relationship between BP and lower limb function was not found (results not shown).

**DISCUSSION**

We tested whether higher BP would be associated with more gait difficulties in 888 older persons examined

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**Figure 1.** Lower limb function over time as a function of systolic blood pressure (SBP). Figure shows the generalized estimating equation model of the $z$ score composite measure of lower limb function by study year in three groups of participants with different SBPs: SBP = 120 mmHg (solid line), SBP = 135 mmHg (dotted line), and SBP = 160 mmHg (dashed line). Change in lower limb function per year is $-1.13 \times 10^{-1}$ for a baseline SBP of 160 mmHg, $-9.79 \times 10^{-2}$ for a baseline SBP of 135 mmHg, and $-8.84 \times 10^{-2}$ for a baseline SBP of 120 mmHg.
decline in lower extremity motor function 3 years later. However, by describing change in lower limb function with only two time points, it was difficult to separate initial level of function from the estimate of change (30). Also, the composite BP measure limited the ability to determine if the BP effect was related to SBP, DBP, or antihypertensive medication use. Our analyses were able to address these issues. Participants completed a mean of nearly eight annual evaluations with a high rate of follow-up, enhancing our ability to model change. Of the three BP representations, we found that elevated SBP had the most consistent effect on lower limb function decline. We were able to show that a 10 mmHg increase in SBP and SBP >160 mmHg each were associated with decline in lower limb function. DBP >90 mmHg (rather than a continuous measure) was associated with decline in lower limb function. Use of medications with antihypertensive properties was not associated with lower limb function decline.

Why SBP predicts decline in lower limb function is uncertain. A priori, stroke was hypothesized to mediate the relationship between BP and lower limb function decline. Although baseline clinical stroke had no effect on higher SBP being associated with lower limb function decline, censoring individuals who developed stroke reduced the estimate of interaction and statistical significance of the association. Therefore, clinical stroke (which mainly captures strategic cerebral infarction) may be a mechanism by which SBP causes decline in lower limb function. In addition, elevated BP has been associated with increased periventricular and subcortical white matter changes on neuroimaging (25,26), and prior studies have shown that white matter changes are associated with gait (11,12). Determining whether these chronic ischemic changes also mediate the association between BP and decline in lower limb function will require investigations using either imaging or pathology data.

Confidence in our findings is strengthened by using a previously established composite measure of lower limb function. Also, the relatively large size of the cohort enhanced our ability to identify an association between BP and lower limb function even after controlling for vascular disease, diabetes, and cognition.

Use of multiple BP readings prior to measuring change in lower limb function rather than just baseline BP would have strengthened our finding that late-life SBP is associated with lower limb function decline. However, BP readings prior to baseline were not available for the Rush Religious Orders Study cohort. Further studies examining lifelong BP measures will be necessary to fully explore the mechanisms by which BP is associated with lower limb function. Also, the Rush Religious Orders Study participants are selected and differ from the general population in education and lifestyle. Studies of BP and gait in defined populations are needed.

Decline in lower limb function is common in older people, and worsening gait is associated with increased risk of dementia and death. Our results suggest that late-life SBP may play a role in lower limb function decline. However, our findings need confirmation, and the mechanism of this association must be understood before lifestyle and medication interventions can be considered.

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Table 2. Relationship of Blood Pressure and Use of Medications With Antihypertensive Properties With Baseline and Annual Rate of Change in Lower Limb Function*
REFERENCES


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