Pulse Wave Velocity and Cognitive Decline in Elders
The Health, Aging, and Body Composition Study

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Background and Purpose—Arterial stiffness is a measure of subclinical cardiovascular disease and increases with age. This study examines the association between arterial stiffness and cognitive decline in a cohort of older adults.

Methods—A total of 2488 subjects with baseline measure of arterial stiffness (mean age, 74.2 years; 52.3% women) were prospectively followed over 9 years in the Health, Aging, and Body Composition Study. Arterial stiffness was measured as pulse wave velocity (PWV) and analyzed in tertiles. Cognitive function was assessed using the Modified Mini-Mental State examination at baseline and repeated at years 3, 5, 8, and 10. Lower Modified Mini-Mental State examination scores indicate worse function. We fit linear mixed models to examine longitudinal changes in cognitive function over the 9 years of follow-up and logistic regression models, restricted to 1331 participants, to examine cognitive impairment defined as a decrease of ≥5 points after 9 years. We adjusted for sociodemographics, Apoe4, and cardiovascular disease risk factors.

Results—The annual decrease in Modified Mini-Mental State examination scores was 0.30 points at low PWV (95% confidence interval [CI], −0.37 to −0.22), 0.46 points at middle PWV (95% CI, −0.54 to −0.39), and 0.45 points at high PWV (95% CI, −0.53 to −0.38), from fully adjusted linear mixed models. In fully adjusted models, the odds of cognitive impairment after 9 years of follow-up was 40% greater for subjects with middle PWV (odds ratio [OR], 1.40; 95% CI, 1.03–1.92) and 59% greater for subjects with high PWV (OR, 1.59; 95% CI, 1.16–2.18), compared with low PWV.

Conclusions—High arterial stiffness was modestly associated with cognitive decline and impairment. Interventions to prevent arterial stiffness may be effective in delaying cognitive decline. (Stroke. 2013;44:388-393.)

Key Words: arterial stiffness ■ cognitive impairment ■ epidemiology ■ hypertension

Arterial stiffness is a measure of subclinical cardiovascular disease (CVD) risk that progressively increases with age. Arterial stiffness largely contributes to systolic hypertension, the most common form of hypertension among older adults. Independent of traditional CVD risk factors, arterial stiffness has been linked to damages in the central pulse pressure resulting in cerebral microvascular disease and changes in the functioning of the frontal–subcortical regions of the brain which may, in turn, influence cognitive decline.

Cross-sectional studies have demonstrated an association between high pulse wave velocity (PWV) and poor cognitive performance. However, the prospective association between PWV and cognitive decline has not yet been established, and findings have been inconsistent. For example, results from the Rotterdam study did not provide evidence for an association between PWV and cognitive decline. On the contrary, results from the Baltimore Longitudinal Study of Aging suggested significant associations between higher PWV and more rapid cognitive decline on specific cognitive domains, such as working memory, but not on tests of global cognitive function.

Using data from the Health, Aging, and Body Composition (Health ABC) Study, a biracial prospectively followed cohort of older adults who were initially free of functional limitations, we examined associations between baseline arterial stiffness and change in cognitive function over 9 years of follow-up.

Methods

Study Population

Participants in this analysis were from Health ABC, a prospective cohort study of 3075 community-dwelling elders 70 to 79 years of age at baseline in 1997. Health ABC is a biracial cohort of whites and blacks. Potential participants were living in either Memphis, TN, or Pittsburgh, PA. Further details on the study design and recruitment...
strategy have been published elsewhere. Clinical and biological data were collected annually from years 1 through 6 and biennially through year 10. A total of 2488 participants had a measurement of arterial stiffness at baseline and thus constituted our analytic cohort.

Assessment of Cognitive Function
Cognitive function was assessed using the Modified Mini-Mental State (3MS) examination, a 100-point assessment of global cognitive function. The 3MS examination has greater sensitivity and specificity and fewer floor and ceiling effects for detecting impairment than other measures, such as the Mini-Mental State examination, and has excellent test-retest properties. Lower scores denote worse cognitive function. The 3MS examination was administered at baseline (year 1) and in years 3, 5, 8, and 10.

Assessment of Arterial Stiffness
PWV, a measure of arterial stiffness, was assessed at year 1 examination using nondirectional transcutaneous Doppler flow probes (model 810-a, 10 MHz; Parks Medical Electronics, Aloha, OR). PWV is regarded as the gold standard measure of arterial stiffness and a more direct measure than pulse pressure. For each participant, 3 runs, each with a minimum of 10 pairs of simultaneous flow waves from the right carotid and right femoral arteries, were recorded and then averaged. The distance between the carotid and femoral arteries was measured above the body surface using a metal tape. The time from the R wave on the ECG to the foot of the pressure wave was also calculated. Both components were then used to calculate PWV as the distance between the carotid and femoral arteries divided by the time differential for the pressure wave to reach both arteries. Our measure of PWV shows an interclass correlation of 0.88 between sonographs and 0.84 between readers. The latter was based on repeated PWV measures from a random sample of 14 participants. Higher PWV (in cm/s) indicates greater stiffness of the vessels. When compared with participants with PWV measure, those without PWV measure were younger, had lower education, and lower baseline 3MS examination score but did not differ with regard to cardiovascular risk factors, such as body mass index (BMI), prevalence of hypertension, and type2 diabetes mellitus.

Covariates
We examined other covariates that were measured during the base-line examination. Participants self-reported their race/ethnicity (white or black), age, sex, and years of education completed (less than high school, high school graduate, and postsecondary). Participants also reported their alcohol consumption and current smoking status. BMI (in kg/m²) was determined from measured weight and height and calculated as weight in kg/height in m². Levels of lipids, including high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (mg/dL), were measured from fasting blood drawn at baseline. Collected blood was processed, then frozen samples were shipped to Health ABC laboratory for analysis. The presence of type 2 diabetes mellitus was ascertained as a combination of self-report of a physician diagnosis, use of diabetes mellitus medication, or the following laboratory value (fasting glucose level ≥126 mg/dL or a 2-hour oral glucose tolerance test >200 mg/dL). History of myocardial infarction was ascertained based on self-report of a physician diagnosis or hospitalization. Systolic and diastolic blood pressures were measured twice, then averaged. Hypertension was ascertained as a self-report of a physician diagnosis, use of medication, a systolic blood pressure >140 mm Hg, or a diastolic blood pressure >90 mm Hg. Mean arterial blood pressure was determined from measured systolic and diastolic blood pressures as diastolic pressure +1/3 (systolic pressure-diastolic pressure). Depressive symptoms were assessed using the 20-item Center for Epidemiological Studies Depression Scale ranging from 0 to 60 with higher scores denoting worse depressive symptoms. Having elevated depressive symptoms was defined as a Center for Epidemiological Studies Depression score ≥16. The Center for Epidemiological Studies Depression scale has high validity and reliability when administered to community-dwelling older adults.

Statistical Analyses
To allow for nonlinear response and for ease of interpretation, we categorized PWV into tertiles, the main predictor of interest. In bivariate analyses, we used t test and analysis of variance to examine the distribution of baseline covariates across tertiles of PWV (Table 1). We examined the longitudinal associations between tertiles of PWV and cognitive decline over the 9 years of follow-up using linear mixed models with random slopes and intercepts (Table 2). In linear mixed models, the outcome includes all available repeated measures of 3MS examination. We operationalized time as age at time of cognitive assessment, which we then grand-mean centered (mean age, 74.2 years). We included a PWV by age interaction to estimate PWV-related cognitive decline. We reported the annual change in the 3MS examination scores according to tertiles of PWV (estimate and 95% confidence interval [CI]). In the Figure, we illustrated the multivariate-adjusted associations between tertiles of PWV and longitudinal change in 3MS examination scores over time (as age), based on the results from linear mixed models. We also fit logistic regression models (Table 3) to examine the association between tertiles of PWV and cognitive impairment, which we defined as a decrease of 5 or more points on the 3MS examination between baseline and year 10 examinations (N=1331). We reported odds ratios (ORs) and 95% CIs. In multivariate models, we adjusted for potential confounders, including race/ethnicity, sex, education, ApoE4 allele, and traditional CVD risk factors, such as BMI, type2 diabetes mellitus, hypertension, and mean arterial blood pressure. Selection of covariates was based on previous literature and the association of covariates with PWV and cognitive function. We conducted all analyses using SAS v.9.2.

Results
Higher PWV was associated with greater age at enrollment, being male, black, having less education, higher BMI, lower high-density lipoprotein, higher mean arterial blood pressure, type2 diabetes mellitus, myocardial infarction, hypertension, and lower cognitive score (Table 1).

Results from linear mixed models of the associations between tertiles of PWV and change in cognitive scores over the 9 years of follow-up are presented in Table 2. All models included PWV tertiles, age, and PWV by age interactions, indicating PWV-related cognitive decline. We presented the results as annual change in the 3MS examination score associated with tertiles of PWV. In model 1, the annual decrease in 3MS examination scores was 0.32 points for participants with low PWV (95% CI, −0.40 to −0.25), annual decrease of 0.49 points at middle PWV (95% CI, −0.56 to −0.41), and an annual decrease of 0.45 points at high PWV (95% CI, −0.53 to −0.37). Adjusting for sociodemographics (model 2), ApoE4 allele and CVD risk factors (model 3) slightly attenuated the associations but remained significant.

The multivariable-adjusted associations between tertiles of PWV and age-related cognitive decline are illustrated in the Figure, based on results from linear mixed models. For example, over 9 years of follow-up, participants with the high and middle tertiles of PWV experienced an average decline in 3MS examination scores of ≈4.5 points versus 2.9 points for those with the lowest tertile of PWV.

We performed exploratory analysis to examine whether higher PWV was associated with decline on specific cognitive domains of the 3MS examination (data not shown). We created composite scores pertaining to 4 cognitive domains: memory, executive function, language, and visuospatial. Our findings suggested that higher PWV was modestly associated with
greater decline on visuospatial and language tasks \((P<0.05)\) but not on executive function or memory tasks.

Results from logistic regression models of the associations between tertiles of PWV and odds of cognitive impairment after 9 years of follow-up included a total of 1331 participants who completed both baseline and year 10 cognitive assessments (Table 3). Of the 1331 participants, a total of 409 (30.7%) experienced a decrease of 5 or more points in their 3MS examination score at year 10, and thus are considered cognitively impaired. In unadjusted models and compared with subjects with low PWV, those with middle PWV had 50% greater odds of cognitive impairment (OR, 1.50; 95% CI, 1.13–1.99) and those with high PWV had 63% greater odds of cognitive impairment (OR, 1.63; 95% CI, 1.22–2.19). Adjusting for sociodemographics (model 2), Apoe4 allele and cardiovascular risk factors (model 3) slightly attenuated the associations but remained significant. In fully adjusted models and compared with participants with low PWV, those with middle PWV had 40% greater odds of cognitive impairment (OR, 1.40; 95% CI, 1.03–1.92), and those with high PWV had 59% greater odds of impairment (OR, 1.59; 95% CI, 1.16–2.18).

Table 1. Baseline Characteristics of the Study Population by Tertile of Pulse Wave Velocity, Health, Aging, and Body Composition Study (N=2488).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall</th>
<th>Low (PWV&lt;6.5 cm/s)</th>
<th>Middle (6.5–6.9 cm/s)</th>
<th>High (6.9–8.0 cm/s)</th>
<th>(p) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>74.2 (2.9)</td>
<td>73.9 (2.8)</td>
<td>74.3 (2.9)</td>
<td>74.4 (2.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Women, no., %</td>
<td>1302 (52.3)</td>
<td>481 (58.0)</td>
<td>425 (61.2)</td>
<td>396 (47.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Black, no., %</td>
<td>1002 (40.3)</td>
<td>296 (35.7)</td>
<td>348 (41.9)</td>
<td>358 (43.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>&lt;High school education, no., %</td>
<td>575 (23.1)</td>
<td>151 (18.2)</td>
<td>222 (26.8)</td>
<td>202 (24.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>&gt;1 alcohol drink/d, no., %</td>
<td>196 (7.9)</td>
<td>74 (8.9)</td>
<td>60 (7.2)</td>
<td>62 (7.5)</td>
<td>0.38</td>
</tr>
<tr>
<td>Current smoker, no., %</td>
<td>254 (10.2)</td>
<td>75 (9.1)</td>
<td>89 (10.7)</td>
<td>90 (10.9)</td>
<td>0.39</td>
</tr>
<tr>
<td>BMI, mean (SD), kg/m²</td>
<td>27.4 (4.8)</td>
<td>26.5 (4.6)</td>
<td>27.9 (4.8)</td>
<td>27.8 (4.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Low-density lipoprotein, mean (SD), mg/dL</td>
<td>121.8 (34.7)</td>
<td>121.3 (33.0)</td>
<td>121.9 (34.9)</td>
<td>122.1 (36.1)</td>
<td>0.87</td>
</tr>
<tr>
<td>High-density lipoprotein, mean (SD), mg/dL</td>
<td>54.5 (17.0)</td>
<td>56.7 (16.7)</td>
<td>53.6 (16.7)</td>
<td>53.2 (17.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Triglycerides, mean (SD), mg/dL</td>
<td>139.9 (84.6)</td>
<td>134.7 (93.1)</td>
<td>142.8 (83.7)</td>
<td>142.0 (76.0)</td>
<td>0.10</td>
</tr>
<tr>
<td>Arterial BP, mean (SD), mmHg</td>
<td>93.4 (12.7)</td>
<td>91.0 (11.7)</td>
<td>93.4 (12.9)</td>
<td>95.8 (13.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes mellitus, no., %</td>
<td>567 (22.8)</td>
<td>121 (14.6)</td>
<td>188 (22.7)</td>
<td>258 (31.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Myocardial infarction, no., %</td>
<td>300 (12.1)</td>
<td>87 (10.5)</td>
<td>100 (12.1)</td>
<td>113 (13.6)</td>
<td>0.15</td>
</tr>
<tr>
<td>Hypertension, no., %</td>
<td>1512 (60.8)</td>
<td>414 (49.9)</td>
<td>506 (61.0)</td>
<td>592 (71.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CESD ≥16, no., %</td>
<td>93 (3.7)</td>
<td>37 (4.5)</td>
<td>33 (4.0)</td>
<td>23 (2.8)</td>
<td>0.18</td>
</tr>
<tr>
<td>Apolipoprotein 4, no., %</td>
<td>667 (26.8)</td>
<td>214 (27.0)</td>
<td>233 (29.6)</td>
<td>220 (27.5)</td>
<td>0.46</td>
</tr>
<tr>
<td>3MS examination score, mean (SD)</td>
<td>90.4 (8.1)</td>
<td>91.2 (7.9)</td>
<td>90.2 (8.2)</td>
<td>89.6 (8.2)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

3MS indicates Modified Mini-Mental State; BMI, body mass index; BP, blood pressure; and CESD, Center for Epidemiological Studies Depression Scale.

*pulse wave velocity data were log transformed and categorized into tertiles: low, 5.7 to 6.5 cm/s; middle, 6.5 to 6.9 cm/s; and high, 6.9 to 8.0 cm/s.

Table 2. Annual Change in the Modified Mini-Mental State Examination According to Tertile of Pulse Wave Velocity From Linear Mixed Models, Health, Aging, and Body Composition Study

<table>
<thead>
<tr>
<th>PWV Tertile</th>
<th>Model 1 Estimate (95% CI)</th>
<th>Model 2 Estimate (95% CI)</th>
<th>Model 3 Estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>(-0.32 ) ((-0.40 \text{ to } -0.25))</td>
<td>(-0.31 ) ((-0.39 \text{ to } -0.24))</td>
<td>(-0.30 ) ((-0.37 \text{ to } -0.22))</td>
</tr>
<tr>
<td>Middle</td>
<td>(-0.49 ) ((-0.56 \text{ to } -0.41))</td>
<td>(-0.47 ) ((-0.55 \text{ to } -0.40))</td>
<td>(-0.46 ) ((-0.54 \text{ to } -0.39))</td>
</tr>
<tr>
<td>High</td>
<td>(-0.45 ) ((-0.53 \text{ to } -0.37))</td>
<td>(-0.45 ) ((-0.53 \text{ to } -0.38))</td>
<td>(-0.45 ) ((-0.53 \text{ to } -0.38))</td>
</tr>
</tbody>
</table>

Model 1 was age-adjusted and included PWV by age interactions; Model 2 was additionally adjusted for race, sex, and education; Model 3 was additionally adjusted for APOE4, body mass index, high-density lipoprotein, diabetes mellitus, hypertension, and mean arterial blood pressure. CI indicates confidence interval; and PWV, pulse wave velocity.

Figure. Multivariate-adjusted longitudinal changes in performance on the Modified Mini-Mental State (3MS) examination as a function of tertiles of pulse wave velocity (PWV, cm/s). The overall probability value for tertiles of PWV by age interaction is <0.01. These associations were assessed in linear mixed models, adjusted for age, sex, race/ethnicity, education, Apoe4, body mass index, diabetes mellitus, hypertension, and mean arterial blood pressure. Lower scores on the 3MS examination indicate worse cognitive performance.
events and CVD risk factors, which, in turn, are important also been demonstrated as an independent predictor of CVD with cognitive impairment. Finally, arterial stiffness has white matter hyperintensities, which, in turn, are associated imaging studies have increasingly linked arterial stiffness to inconsistent conclusions. Our study findings were inconsistent conclusions. Previous literature suggests that blacks have greater arterial stiffness, higher prevalence of hypertension, and exhibit lower rates of blood pressure control than non-Hispanic whites. Although previous epidemiological studies, such as the Baltimore Longitudinal Study of Aging, included whites and blacks, their small sample size with available PWV measurement (N=582) may have hindered their statistical power to examine any racial/ethnic-related disparity. As an exploratory analysis, we examined whether the association between arterial stiffness and cognitive decline differed for our white (n=1486) and black (n=1002) participants. Although blacks had lower cognitive scores at baseline than whites, the rates of cognitive decline associated with arterial stiffness did not differ by race/ethnicity (P>0.05). Future studies need to confirm our findings. Our study is the first population-based study to examine the association between arterial stiffness and cognitive decline in a large cohort of community-dwelling older adults who underwent >2 repeated cognitive assessments and over a long period of follow-up. Furthermore, our study extends the literature by examining racial/ethnic-related disparity in the longitudinal association of arterial stiffness with cognitive decline, which other studies did not examine, possibly because of lack of statistical power. As such, our study has several strengths, including the large sample size of a biracial community-dwelling cohort of older adult whites and blacks who were well functioning at baseline. Participants in this study were prospectively followed over a long study period with repeated measures of cognitive testing. Finally, PWV is regarded as the gold standard for measuring arterial stiffness and thus provides a great strength to our study. Our study findings were consistent with previous studies demonstrating a cross-sectional association between arterial stiffness and cognitive impairment. Importantly, however, only a handful studies documented the longitudinal associations between arterial stiffness and cognitive decline and reported inconsistent conclusions. Our study findings were inconsistent with those among older adults of the Rotterdam study, which did not provide evidence for a prospective association between PWV and cognitive decline, measured across 2 study time points only. Our findings were in accordance with those from the Baltimore Longitudinal Study of Aging (N=582), which found significant associations between higher PWV and more rapid cognitive decline on the Mini-Mental Status examination over 1-year follow-up only. Further results from our exploratory analyses suggested that higher PWV, suggestive of increased vascular risk, may be more associated with deteriorations in language and visual–spatial tasks than in memory or executive function tasks. Our findings confirm that higher arterial stiffness, as measured by PWV, is associated with faster rates of cognitive decline over 9 years of follow-up and with greater odds of cognitive impairment among community-dwelling older adults, beyond traditional cardiovascular risk factors, such as BMI, type2 diabetes mellitus, hypertension, and mean arterial blood pressure. Several pathways linking arterial stiffness and cognitive decline have been postulated. First, when arteries undergo stiffness, they often result in damages to pressure pulsatility. The increase in central pulse pressure results in hemodynamic stress in the heart and in high-flow end organs, such as the brain, to which it is transmitted. The high levels of central pulse pressure in the brain result in structural changes and dysfunction to its microcirculation. Second, high pulse pressures may result in structural changes to cerebral blood vessels, which may, in turn, interfere with the transport of important nutrients to the brain and interfere with the clearance of toxic byproducts out of the brain. Third, recent brain imaging studies have increasingly linked arterial stiffness to cerebral microvascular disease and changes in the functioning of the frontal–subcortical regions of the brain, such as white matter hyperintensities, which, in turn, are associated with cognitive impairment. Finally, arterial stiffness has also been demonstrated as an independent predictor of CVD events and CVD risk factors, which, in turn, are important predictors of cognitive decline. Our study findings were consistent with previous studies demonstrating a cross-sectional association between arterial stiffness and cognitive impairment. Importantly, however, only a handful studies documented the longitudinal associations between arterial stiffness and cognitive decline and reported inconsistent conclusions. Our study findings were in accordance with those from the Baltimore Longitudinal Study of Aging (N=582), which found significant associations between higher PWV and more rapid cognitive decline on the Blessed Information Memory Concentration Test (working memory test). However, results from the Baltimore Longitudinal Study of Aging did not provide evidence for an association between PWV and tests of global cognitive function. Previous results from a subsample (N=552) of older adults in Health ABC provided an association between higher PWV and greater cognitive decline on the psychomotor speed only, but not on tests of memory and global cognitive function. Finally, recent findings from the PARTAGE study, among 873 institutionalized patients ≥80 years of age living in France and Italy, showed an association between higher tertile of PWV and greater cognitive decline on the Mini-Mental Status examination over 1-year follow-up only. Further results from our exploratory analyses suggested that higher PWV, suggestive of increased vascular risk, may be more associated with deteriorations in language and visual–spatial tasks than in memory or executive function tasks.

### Discussion

Our findings confirm that higher arterial stiffness, as measured by PWV, is associated with faster rates of cognitive decline over 9 years of follow-up and with greater odds of cognitive impairment among community-dwelling older adults, beyond traditional cardiovascular risk factors, such as BMI, type2 diabetes mellitus, hypertension, and mean arterial blood pressure. Several pathways linking arterial stiffness and cognitive decline have been postulated. First, when arteries undergo stiffness, they often result in damages to pressure pulsatility. The increase in central pulse pressure results in hemodynamic stress in the heart and in high-flow end organs, such as the brain, to which it is transmitted. The high levels of central pulse pressure in the brain result in structural changes and dysfunction to its microcirculation. Second, high pulse pressures may result in structural changes to cerebral blood vessels, which may, in turn, interfere with the transport of important nutrients to the brain and interfere with the clearance of toxic byproducts out of the brain. Third, recent brain imaging studies have increasingly linked arterial stiffness to cerebral microvascular disease and changes in the functioning of the frontal–subcortical regions of the brain, such as white matter hyperintensities, which, in turn, are associated with cognitive impairment. Finally, arterial stiffness has also been demonstrated as an independent predictor of CVD events and CVD risk factors, which, in turn, are important predictors of cognitive decline. Our study findings were consistent with previous studies demonstrating a cross-sectional association between arterial stiffness and cognitive impairment. Importantly, however, only a handful studies documented the longitudinal associations between arterial stiffness and cognitive decline and reported inconsistent conclusions. Our study findings were in accordance with those from the Baltimore Longitudinal Study of Aging (N=582), which found significant associations between higher PWV and more rapid cognitive decline on the Blessed Information Memory Concentration Test (working memory test). However, results from the Baltimore Longitudinal Study of Aging did not provide evidence for an association between PWV and tests of global cognitive function. Previous results from a subsample (N=552) of older adults in Health ABC provided an association between higher PWV and greater cognitive decline on the psychomotor speed only, but not on tests of memory and global cognitive function. Finally, recent findings from the PARTAGE study, among 873 institutionalized patients ≥80 years of age living in France and Italy, showed an association between higher tertile of PWV and greater cognitive decline on the Mini-Mental Status examination over 1-year follow-up only. Further results from our exploratory analyses suggested that higher PWV, suggestive of increased vascular risk, may be more associated with deteriorations in language and visual–spatial tasks than in memory or executive function tasks.

### Conclusion

In this cohort of community-dwelling older adults, we provided evidence of an association between higher arterial stiffness and
greater cognitive decline and impairment, beyond traditional cardiovascular risk factors. PWV may, therefore, constitute a useful and noninvasive measure in predicting the risk of cognitive decline among older adults. Our results from this longitudinal study suggest that interventions to prevent arterial stiffness may be effective in delaying cognitive decline. Further prospective studies need to confirm our longitudinal results of the association of arterial stiffness and cognitive decline in older adults.

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References
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Abstract

背景および目的: 労動の硬化は無症状性循環器疾患の尺度の1つで, 年齢とともに進行する。本試験は, 高齢者コホートで動脈の硬化と認知機能低下の関係を調べた。

方法: Health, Aging, and Body Composition Study では, ベースライン時に動脈の硬化性を測定した2,488例（平均年齢74.2歳; 其のうち男性は52.3％）を9年間にわたり前向きに追跡した。脈波伝播速度（PWV）により動脈の硬化を測定し, 測定値を3群に分けて分析した。ベースライン時、3年目、5年目、8年目、および10年日に修正ミニメンタルステート検査を行い、認知機能を評価した。修正ミニメンタルステート検査のスコアが高い場合は、認知機能障害を意味する。9年間の経過観察における認知機能の長期変化を調べるために線形混合法モデルを用い、1,331例に限定して9年後に5点以上減少した参加者を認知障害と診断した。社会人口統計学、Apoe4、および心循環器疾患の危険因子による調整を施した。

結果：修正ミニメンタルステート検査のスコアは、PWVが低い被験者では1年間で完全調整済み線形混合法モデルから0.30点（95％信頼区間（CI）：−0.37～−0.22）減少しており、中等度の被験者では0.46点（95％CI：−0.54～−0.39）、高値の被験者では0.45点（95％CI：−0.53～−0.38）減少した。完全調整済みモデルでは、9年間の経過観察後の認知障害の可能性はPWVが低い被験者と比較して、中等度のPWVの被験者で40％大きく（オッズ比（OR）=1.40；95％CI：1.03～1.92）、PWVが高い被験者では59％大きい（OR=1.59; 95％CI:1.16～2.18）ことが明らかになった。

結論: 重度の動脈硬化性は認知機能低下および認知障害をある程度伴うことが多い。動脈硬化性を予防する治療が認知機能の低下を遅らせるために有効かもしれない。

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表3
The Health, Aging, and Body Composition Studyの9年間の経過観察後の脈波伝播速度を3群に分けて実施した修正ミニメンタルステート検査に及ぼす認知障害のリスク。

<table>
<thead>
<tr>
<th>模型</th>
<th>PWV3群 OR (95% CI)</th>
<th>モデル2 OR (95% CI)</th>
<th>モデル3 OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>低値（基準値）</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>中等度</td>
<td>1.50(1.13～1.99)</td>
<td>1.34(0.99～1.79)</td>
<td>1.40(1.03～1.92)</td>
</tr>
<tr>
<td>高値</td>
<td>1.63(1.22～2.19)</td>
<td>1.48(1.09～2.00)</td>
<td>1.59(1.16～2.18)</td>
</tr>
</tbody>
</table>

5点以上の低下がある場合、認知障害と診断する。モデル1は未調整、モデル2は年齢、性別、人種、および教育で調整、モデル3は、これらに加えて、Apoe4、BMI、HDL、糖尿病、高血圧症および平均脈圧で調整した。CI:信頼区間, OR:オッズ比, PWV:脈波伝播速度。