Higher Aortic Stiffness Is Associated With Lower Global Cerebrovascular Reserve Among Older Humans

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Abstract—Greater aortic stiffness and pulse pressure are associated with cerebrovascular remodeling, reduced white matter microstructure, and cognitive performance with aging in humans. However, it is unclear whether aortic stiffness and pulse pressure are associated with reduced basal global cerebral blood flow (CBF) and cerebrovascular reserve among older adults. Global CBF was quantified in 205 adults (range, 19–87 years; mean±SE: 30.6±1.3 years) using quantitative [^{15}O] water brain positron emission tomography imaging. In a subset of older adults (n=24; 70.0±2.0 years), aortic stiffness (carotid femoral pulse wave velocity) and cerebrovascular reserve (change in global CBF after intravenous infusion of acetazolamide) were assessed. In the entire cohort, global CBF was lower in older compared with young adults (36.5±1.1 versus 50.5±0.7 mL/min per 100 mL; P<0.001). Global CBF was higher in young women compared with young men (51.0±0.30 versus 47.4±0.03 mL/min per 100 mL; P<0.001) but did not differ between older women and men (P=0.63). In older adults, greater carotid femoral pulse wave velocity was associated with lower cerebrovascular reserve (r=−0.68; P=0.001 adjusted for age, sex, and mean arterial pressure) but not global CBF (r=0.13; P=0.60). Brachial pulse pressure was not associated with lower cerebrovascular reserve (r=−0.37; P=0.159) when adjusted for age and sex. These data indicate that the age-related increases in aortic stiffness may contribute, in part, to the brain's impaired ability to augment blood flow in response to a stimulus with aging in humans. **(*Hypertension*. 2018;72:476-482. DOI: 10.1161/HYPERTENSIONAHA.118.11143.)** ● **Online Data Supplement**

Key Words: acetazolamide ■ aging ■ arterial pressure ■ positron emission tomography

Heart disease, stroke, and dementia continue to be the number 1, 5, and 6 leading causes of death, respectively, in individuals >65 years of age in the United States (Center of Disease Control). Dementia, characterized by a decline in cognitive ability sufficient to interfere with daily life, results in substantial emotional and financial burdens to the patient, caregiver, and community. Health care costs associated with dementia are estimated to be ≈60% higher than costs associated with heart disease or cancer and are expected to climb as the prevalence of dementia surges from 5 million to >14 million by 2050 (National Institutes of Health, Alzheimer's Association). Although the mechanisms that contribute to dementia remain unclear, attention has shifted from the solitary amyloid hypothesis toward a complex cause that acknowledges the vascular contribution in the pathogenesis of mild cognitive impairment and dementia, including Alzheimer disease.[1–3] In support of this paradigm shift, there is extensive overlap between traditional cardiovascular disease and cerebrovascular disease risk factors, such as older age, hypertension, diabetes mellitus, higher body mass index, and increased risk of cognitive impairment and dementia. More recently, elevated aortic stiffness has been identified as a novel risk factor associated with cognitive impairment among older adults with and without hypertension independent of other cardiovascular disease risk factors.[4–6] However, the mechanisms by which aortic stiffness contributes to cognitive decline with advancing age remain poorly understood.

Aortic stiffness, determined by carotid femoral pulse wave velocity (cfPWV), is an independent predictor of cardiovascular disease events in older adults without cardiovascular disease at baseline.[7] Aortic stiffness and related central hemodynamics are associated with reductions in cognitive performance on memory, processing speed, and executive function tasks.[4,8–11] Importantly, longitudinal increases in aortic stiffness are associated with declines in cognitive performance over the lifespan.[5] Stiffening of the aorta reduces the ability of aorta to buffer pulsatile blood flow from the left ventricle during systole, resulting in elevated central systolic blood pressure (BP) and pulse pressure (PP). Furthermore, augmented aortic stiffness reduces the mismatch between the low impedance (central elastic arteries) and high impedance (peripheral muscular) arteries, thereby increasing transmission of pulsatile energy to the low resistance cerebrovasculature of high flow organs, such as the brain.[4] In this regard, elevated aortic stiffness and pulsatility are hypothesized to contribute, in part,

Received March 8, 2018; first decision March 20, 2018; revision accepted May 23, 2018.

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The online-only Data Supplement is available with this article at http://hyper.ahajournals.org/lookup/suppl/doi:10.1161/HYPERTENSIONAHA.118.11143/-/DC1.

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to declines in cognitive performance with aging by promoting the development of subcortical white matter hyperintensities via increased cerebrovascular remodeling and resistance.[12,13]

In addition, the link between age-related aortic stiffness and pulsatility with cerebral blood flow (CBF) and cerebrovascular reactivity, defined as the ability to augment brain blood flow in response to a vasodilatory stimulus, remains relatively unexplored. Experimentally, cerebrovascular reactivity is quantified by measuring cerebrovascular reserve (CVR) in response to a physiological or pharmacological stimuli, such as CO_2 or acetazolamide (ACZ), a carbonic anhydrase inhibitor. Previous studies demonstrate that nonlinear increases in central PP with advancing age were associated with increases in systolic and pulsatile CBF velocity, independent of age, age,[2] and sex in older adults.[13] In contrast, the relationship between cfPWV and CBF remains unclear with some studies demonstrating associations between cfPWV with selective regional reductions in CBF[14,15] but not with global CBF (gCBF).[13] In addition, brachial-ankle PWV, a composite measure of peripheral and central arterial stiffness, was associated with lower CVR in response to a physiological CO_2 stimulus but not basal CBF estimated by transcranial Doppler.[16] However, the degree to which age-related increases in aortic stiffness are associated with reduced gCBF or CVR using gold-standard measurements of CBF, specifically, [^{15}O]water positron emission tomography (PET) imaging, is unknown. Thus, properly characterizing the nature of the relations between CVR and aortic stiffness and PP with quantitative assessments of CBF is clinically important because reductions in CVR predicts cognitive decline, including the conversion from mild cognitive impairment to dementia.[17,18] Therefore, we hypothesized that higher aortic stiffness and PP would be independently associated with lower gCBF and reduced CVR among older adults.

Methods

Data, Analytic Methods (Code), and Research Materials Transparency

The data that support the findings of this study are available from the corresponding author on reasonable request.

Subjects

One hundred and sixty-five young (age: 19–37 years) and 40 older adults (age: 55–87 years) were recruited between the years 2006 and 2016 from the Iowa City, Iowa community, and the University of Iowa Hospital and Clinics through flyers and email advertisements to undergo neuroimaging testing (Figure S1 in the online-only Data Supplement). All participants that were either controls in specific neuroimaging investigations or recruited specifically for a study designed to investigate relationships between vascular function and cognitive performance, gCBF, and CVR in atherosclerotic vascular disease and aging.[19] This latter study involved a subset of 24 older adults (age range: 55–87 years) recruited to complete measurements of aortic stiffness. These individuals were free of major psychiatric illness and neurological diseases except for mild cognitive impairment. Two participants were categorized as mild cognitive impairment based on published criterion from the Alzheimer's Disease Neuroimaging Initiative-2 at the time of PET imaging.

Participants abstained from taking vasoactive medication and antioxidant therapy on the morning of their vascular visit. Female participants in this subset were postmenopausal and not on hormone replacement therapy. The study conformed to the standards sets by the Declaration of Helsinki, and all participants provided written consent to the study, and the protocol was approved by the Institutional Review Board and the Medical Radiation Protection Committee at the University of Iowa.

Measurements

Aortic Stiffness and Hemodynamic Parameters

Aortic stiffness was determined using noninvasive applanation tonometry via pulse wave analysis (NIHem workstation, Cardiovascular Engineering, Inc, Norwood, MA) as previously described.[20] Briefly, femoral and carotid pressure waveforms were collected sequentially using a noninvasive tonometer. The pressure waveform was gated to the R-wave of the ECG to determine the time difference between the foot of the carotid and femoral diastolic pressure waveforms. The distance between the carotid and femoral pulse sites was measured as the distance between the suprasternal notch and the carotid waveform minus the distance from the suprasternal notch to the femoral pulse site to account for parallel transmission. Corrected distances were divided by the carotid and femoral foot-to-foot time delay to calculate cfPWV.

PET Imaging

gCBF and CVR were assessed using quantitative [^{15}O]water PET imaging with arterial blood sampling using methods previously described.[19,21–23] Briefly, all imaging was performed on an ECAT EXACT HR+Scanner (Siemens Medical Solutions USA, Inc, Knoxville, TN). Dynamic imaging (5 s/frame×20 frames) and arterial blood sampling commenced at tracer injection (45–50 mCi per injection) and continued for 100 seconds. Arterial blood was sampled using an online sampler[24] (binned in 1 second intervals). Parametric images were calculated from the activity images (40 second summed images starting immediately post-bolus transit) and the arterial blood curve using the autoradiographic model as implemented by the pixelwise modeling tool of the PMOD suite of tools (PXMOD, PMOD Technologies, Ltd, Zurich, v. 3.7, http:pmod.com/technologies/index.html). Consistent with the brain work, the partition coefficient was assumed to be equal to 0.9. For each injection, the gCBF was quantified by calculating a volume-weighted average of all intracerebral pixels derived from regions-of-interest manually drawn on each image slice of the parametric image. In the entire cohort (n=205), gCBF was calculated as the average of all available gCBF measures (3–8 [^{15}O]water injections of 45–50 mCi per injection per participant) from all studies because gCBF did not statistically differ by task behavior (F=0.08; P=0.922).

In the subset of older adults (n=24), gCBF and CVR were measured while the participants performed a simple counting task. For this task, participants were asked to count from 1 to 3 repetitively for the duration of the 100 second PET scan at approximately a rate of 1 word per second as previously described.[19] Counting is an overlearned, simple cognitive task used to control variability in resting state CBF as a result of extraneous brain processes not of interest and does not augment gCBF. For this subset, anatomic T1-weighted magnetic resonance images were also available. In these participants, anatomically-based volumes-of-interest were derived from the brain parcellation routine of the PMOD Neuro tool (PNeuro, PMOD Technologies, Ltd, Zurich, v. 3.8) on the T1-weighted images and transferred to the coregistered parametric blood flow images. gCBF values were calculated as the volume-weighted average of all volumes-of-interest. Cerebrovascular reactivity was quantified by calculating CVR by comparing gCBF after administration of ACZ (at ≈15 minutes post 1 g IV), a carbonic anhydrase inhibitor to induce maximal vasodilation, to the gCBF determined during the baseline counting task.[22] CVR was calculated as the absolute (absCVR=ACZ flow−basal gCBF) and relative percent change (relCVR[%]=ACZ −basal gCBF/basal gCBF) in all participants. In 19 of the 24 participants, supine brachial BP was recorded during the counting and ACZ [^{15}O] injections using an automated BP cuff (Figure S1).

Statistical Analysis

In the entire cohort (n=205 adults), 2-tailed independent t tests were used to test differences for age (young versus older adults) and sex differences (women versus men; young women versus young men; and older women versus older men) using IBM SPSS 23.0 software (IBM,

Inc, Armonk, NY). One-way ANCOVA was used to test the interaction between age and sex on gCBF in young adults. In the subset of older adults (n=24), partial correlations were used to determine relationships between vascular variables and gCBF, relCVR (%), and absCVR, respectively. cfPWV was adjusted for mean arterial pressure (MAP) in all partial correlational analyses. Older adults in the subset participants (n=24) were recruited to undergo neuroimaging after completion of a separate study investigating vascular function and cognitive performance.[25] Therefore, measurements of arterial stiffness were completed within a median of 24±3.0 months before completion of [^{15}O]water PET imaging. In a separate analysis, we adjusted cfPWV values to account for this time delay between vascular and neuroimaging visits using previously published longitudinal data for predicted yearly change in cfPWV of 0.05 m/s per year.[26] All data were normally distributed, and mean data are presented as mean±SE. Finally, statistical significance was defined as a 2-tailed α level of <0.05.

Results

Participant Characteristics

One hundred and sixty-five young and 40 older participants completed measures of gCBF. Participant characteristics are described in Table 1. Older adults had a higher body mass index (26.5±0.7 versus 27.8±0.7 kg/m^2; *P*=0.003) compared with young adults but did not differ by any other characteristic besides age.

Changes in gCBF With Age

In the entire cohort, gCBF was greater in young compared with older adults (*P*<0.001; Table 1; Figure 1). gCBF was 3.6 mL/min per 100 mL of tissue higher in young women compared with young men (*P*<0.001; Table 2; Figure 2A). Although women tended to be younger than men in the cohort of young adults, the effect of sex on gCBF in young adults remained significant (*P*=0.004) after adjustment for age, and the interaction between sex and age was not significant (*P*=0.84). Interestingly, gCBF did not differ between older men and women (*P*=0.63; Table 2; Figure 2B).

Participant Characteristics of Subset

In the subset of 24 older adults, additional measures of gCBF, CVR, and arterial stiffness were performed. Brachial BPs collected during neuroimaging were available in 19 of the 24 older with cfPWV as indicated in Table 1. On average, participants were older (70.0±2.0 years), highly

Table 1. Participants Characteristics

Variables	Young Adults (n=165)	Older Adults (n=40)	Older Adults Subset With cfPWV (n=24)	*P* Value (Young vs Older, n=40)	*P* Value (Young vs Older Subset, n=24)
Males/females, n/n	99/66	29/11	16/8	0.128	0.361
Age, y	22.6±0.3	68.0±1.6*	70.0±2.0†	<0.001‡	<0.001‡
Body mass index, kg/m^2	25.7±0.3	27.8±0.7*	26.5±0.7	0.003‡	0.359
Education, y	…	…	15.9±0.5	…	…
Atherosclerotic vascular disease, n (%)	…	…	5 (21.7)	…	…
Mild cognitive impairment, n (%)	…	…	2 (8.3)		…
Antihypertensive medication, n (%)	…	…	7 (30.4)	…	…
Aspirin therapy, n (%)	…	…	9 (39.1)	…	…
Statin, n (%)	…	…	6 (26.1)	…	…
Blood pressure and vascular outcomes					
Brachial systolic BP, mm Hg			117.1±2.5	…	…
Brachial diastolic BP, mm Hg			62.8±1.3	…	…
Brachial pulse pressure, mm Hg			54.2±2.6	…	
Carotid femoral PWV, m/s	…	…	10.1±0.5	…	…
Carotid femoral PWV adjusted for delay between neuroimaging and vascular visits, m/s	…	…	10.2±0.5	…	…
Cerebral blood flow					
Basal global CBF, mL/min per 100 mL of tissue	50.5±0.7	36.5±1.1*	35.2±1.5†	<0.001‡	<0.001‡
ACZ flow, mL/min per 100 mL of tissue	…	…	47.2±1.8	…	…
AbsCVR, mL/min per 100 mL of tissue	…	…	11.6±1.2	…	…
RelCVR, %	…	…	36.1±3.4	…	…
Cognitive performance					
Mini Mental State Examination	…	…	28.9±0.4	…	…

Data are mean±SE. Brachial blood pressures and cfPWV were available in n=19 and n=24 participants, respectively. AbsCVR indicates absolute cerebrovascular reserve; ACZ, acetazolamide; BP, blood pressure; CBF, cerebral blood flow; cfPWV, carotid femoral pulse wave velocity; PWV, pulse wave velocity; and RelCVR, relative cerebrovascular reserve.

*P<0.05 older (n=40) vs young.

†P<0.05 subset of older adults with cfPWV (n=24) vs young.

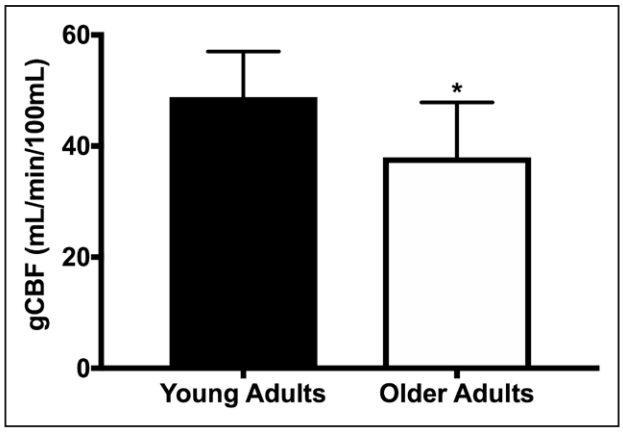

Figure 1. Mean global cerebral blood flow (gCBF) in young (n=165) and older (n=40) adults (n=40). *P<0.05 vs younger. Data are mean±SE.

educated (15.9±0.5 years), and normotensive (brachial systolic BP, 117.1±2.5 mm Hg). Approximately 1 quarter of participants were taking antihypertensive, aspirin, or statin therapy (Table 1). Importantly, older adults imaged as part of this subset are representative of the expected gCBF values based on their age and sex from the entire cohort (n=205). Finally, participants had an average cfPWV of 10.0±0.5 m/s that is within the age-expected normative values of cfPWV.[27]

Relationships Between Aortic Stiffness, BP and gCBF, and CVR

Aortic stiffness, brachial systolic BP, and PP were not associated with basal gCBF and remained nonsignificant after adjustment for age, sex, and MAP (cfPWV only). Bivariate correlations between cfPWV and all BP outcomes were not associated with absCVR or relCVR(%). However, higher cfPWV was strongly correlated with lower absCVR (r=−0.63; P=0.004) after adjustment for age, sex, and MAP. Expressing CVR as a percent change (ie, relCVR%) did not alter the strong association between CVR and cfPWV (Table 3). Brachial systolic BP (r=−0.40, P=0.124; r=−0.21, P=0.443) and PP (r=−0.37, P=0.159; r=−0.15, P=0.585) was not associated with lower absCVR and relCVR(%), respectively (Table 3). Additional adjustment for medication use did not alter findings between cfPWV, absCVR, and CVR%. Finally, associations between cfPWV, basal gCBF, and absCVR were not altered using the predicted cfPWV adjusted for the delay between vascular and neuroimaging visits (Table 3).

Table 2. Basal Global Cerebral Blood Flow Among Men and Women

	Men		Women	
Variable	Young	Older	Young	Older
Global CBF, mL/min per 100 mL of tissue	47.4±0.3	38.3±1.0*	51.0±0.3†	37.3±2.0*

Data are mean±SE. CBF indicates cerebral blood flow.
*Significant (P<0.05) difference between young and older adults.
†Significant (P<0.05) difference between men and women.

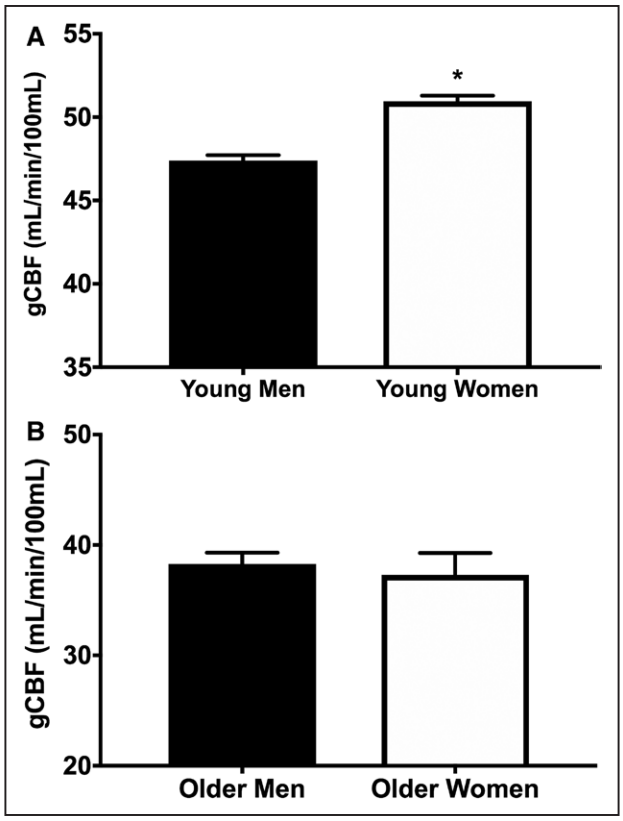

Figure 2. Mean global cerebral blood flow (gCBF) values between (**A**) young men (n=99) and women (n=66) and (**B**) older men (n=29) and women (n=11); *P<0.05 vs younger. Data are mean±SE.

Discussion

The primary novel finding of the present study is that elevated aortic stiffness is strongly associated with lower CVR in older adults, independent of age, sex, and MAP. In contrast, aortic stiffness is not related to basal gCBF in this older cohort. These data are consistent with the hypothesis that increased stiffening of the elastic aorta may contribute, at least in part, to the impaired ability of cerebrovasculature to dilate maximally to augment gCBF in older adults. It is possible that the concomitant rise in aortic stiffness and the loss of impedance mismatch between central and peripheral vasculature result in chronic penetration of augmented forward pulsatile pressure waves to the vulnerable cerebral microvasculature damaging their vasodilatory response.[6] Chronic exposure to pulsatile pressure results in vascular remodeling of the cortical pial and large cerebral arteries,[28] at the expense of cerebral perfusion to the downstream subcortical regions. Although the brain comprises only 2% of the body's total weight, 15% of cardiac output is diverted to the brain to match the high metabolic rate and low energy stores resulting in a coupling of the metabolic demand and the blood flow supply. Interruptions in CBF or even minor decoupling of the demand-supply, such as that by reduced or impaired CVR, may produce ischemic damage to the brain parenchyma and resultant cognitive impairment. Taken together, these data provide an important mechanistic link between elevated aortic stiffness with reductions in white matter microvascular and cognitive performance.[12,29]

Table 3. Partial Correlation Coefficients Between Aortic Stiffness and Blood Pressure Variables With Cerebrovascular Outcomes Among the Subset of Older Adults (n=24)

Variable	cfPWV	Adjusted cfPWV	Brachial Systolic BP	Brachial Diastolic BP	Brachial PP
Global CBF	0.13 (0.60)	0.08 (0.752)	0.10 (0.969)	0.28 (0.269)	−0.14 (0.587)
AbsCVR	−0.63 (0.004)*	−0.61 (0.026)*	−0.40 (0.124)	−0.10 (0.720)	−0.37 (0.159)
RelCVR(%)	−0.63 (0.004)*	−0.60 (0.030)*	−0.21 (0.443)	−0.06 (0.834)	−0.15 (0.585)

Data are partial correlation coefficients (*P* values) adjusted for age and sex. Partial correlations with cfPWV were adjusted for age, sex, and MAP. AbsCVR indicates absolute change in cerebrovascular reactivity; adjusted cfPWV, cfPWV values adjusted for delay between neuroimaging and vascular study visits; BP, blood pressure; CBF, cerebral blood flow; cfPWV, carotid femoral pulse wave velocity; MAP, mean arterial pressure; PP, pulse pressure; and RelCVR(%), relative percent in change in cerebrovascular reactivity.

*Significant ($P<0.05$)

Consistent with other studies,[30–33] gCBF was significantly higher in young compared with older adults. In addition, gCBF was significantly higher in younger women compared with younger men (age <40 years) but did not differ between older men and women. However, we were not sufficiently powered to detect sex differences in gCBF with aging in the present study. Prior studies indicate that the effects of age on sex-related differences in CBF may differ by region and brain matter fiber type.[30,34–37] CBF in the gray matter is significantly greater in women compared with men until the sixth decade of life[33,34,38,39] when losses of vascular and neuroprotective estrogen result in reductions in CBF in postmenopausal women.[40] However, interactions between age and sex on white matter CBF across the lifespan remain unknown. This is clinically significant given the link between elevations in aortic stiffness and development of white matter hyperintensities.[4,41,42] Moreover, because white matter hyperintensities are more prevalent in women compared with men,[43] more studies are needed to better understand the effects of age on differences in CBF between men and women.

Although the measurement of gCBF and CVR in response to ACZ has been performed by others previously,[44–47] this is the first study to investigate the quantitative measurements of gCBF and CVR in relation with aortic stiffness in the same study. Prior studies assessing the relation between vascular function and measures of CBF and CVR have used transcranial Doppler and the functional magnetic resonance imaging method of arterial spin labeling. However, there are known limitations with both methods. Transcranial Doppler used to assess CVR typically measures the change in CBF velocity in the middle cerebral artery, a surrogate marker of CBF, after a physiological stimulus (eg, hypercapnia) under the assumption that hypercapnia does not induce a diameter change in the middle cerebral artery. However, the degree to which transcranial Doppler may underestimate CBF because of dilation of the large cerebral vessels (ie, middle cerebral artery) with hypercapnia remains controversial.[48] Similarly, recent meta-analyses demonstrate that arterial spin labeling magnetic resonance imaging may overestimate gCBF compared with [^{15}O]water PET imaging[49] along with regional and brain matter differences in the CBF estimates between methods.[45,49,50] In addition, the present study induced maximal dilation using the carbonic anhydrase inhibitor, ACZ, to determine CVR. This is important because recent studies demonstrated that the reactivity to a hypercapnic stimulus may be altered in individuals with higher fitness[51] while ACZ reliably produces maximal dilation in humans.[52] Taken together, to the best of our knowledge, this is the first study to assess the true relation between cfPWV and gCBF and CVR using validated measurements of CBF and arterial stiffness.

This study should be interpreted in the context of several limitations. First, our study did not recruit individuals between the ages of 39 and 54 years and therefore is unable to determine the change in gCBF across the entire lifespan (18–87 years), as well as detect the decade in which gCBF no longer differs between men and women. However, in 2 previous studies, CBF was reduced in postmenopausal compared with premenopausal women beyond anticipated age-related changes, suggesting that aging and menopause contribute synergistically toward cerebrovascular changes in postmenopausal women.[40] Second, the sample size of the subset of participants is small, but cfPWV remained significantly associated with CVR even after adjustment for key covariates (age, sex, and MAP), and post hoc power calculation revealed that 99.9% power was achieved. Third, this study did not test cognitive performance and therefore is unable to determine is stiffness-related reductions in CVR are associated with cognitive performance in the subset of older adults. Fourth, central BP was not collected in the subset of 24 older adults. Central PP may more closely represent the BP in which the brain is exposed may be associated with reductions in CBF or CVR not detected by brachial BP measurements in the subset of older adults. Finally, given the cross-sectional design of the present study, we are unable to determine causality between elevated cfPWV and reduced CVR, therefore, cannot rule out a possible bidirectional relation between these outcomes.

In conclusion, elevated aortic stiffness is associated with reductions in CVR among older adults independent of age, sex, and MAP. Furthermore, we confirmed findings from previous smaller studies using [^{15}O]water PET that indeed gCBF is reduced in older compared with younger adults; however, sex differences in gCBF may differ with age. In contrast to our hypothesis, aortic stiffness was not associated with basal gCBF in the present cohort, rather it was associated with the ability of the cerebral vessels to maximally augment CBF suggesting that reduced CVR may be a primary downstream hemodynamic consequence of elevated aortic stiffness. More studies are needed to explore the degree to which elevated aortic stiffness result in regional reductions in CBF and CVR, as well as characterizing these relations across the lifespan.

Perspectives

This study demonstrates that age-related increases in aortic stiffness impair the ability of the cerebrovasculature to dilate in response to physiological or pharmacological stimuli but

does not contribute to age-related reductions in gCBF in older adults. This is clinically significant given the ability of the cerebrovasculature to dilate to physiological stimuli is important in maintaining the coupling of the neurovascular response and is predictive of cognitive decline with aging in humans. Therefore, this study suggests that lower CVR may be an important mechanistic link between elevations in aortic stiffness with alterations in white matter microstructure and cognitive impairment in older adults.

Sources of Funding

This study is supported by National Institutes of Health grants 1R21AG043722 (G.L. Pierce), P01HL014388, R01AG030417 (to D.J. Moser), 1R03AG047306 (L.L. Boles Ponto), U54TR001356 (University of Iowa), American Heart Association 13SDG143400012 (G.L. Pierce), and the Biological Sciences Funding Program (L.L. Boles Ponto) from the University of Iowa Office of the Vice President for Research.

Disclosures

None.

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Novelty and Significance

What Is New?

- In a large cohort using [^{15}O]water positron emission tomography imaging, basal global cerebral blood flow is 3.6 mL/min per 100 mL of tissue lower in older adults compared with young adults.
- Higher aortic stiffness is associated with reduced cerebrovascular reserve but not global cerebral blood flow in older adults.

What Is Relevant?

- Higher aortic stiffness is associated with increased cerebrovascular resistance, reduced white matter microstructure, and cognitive performance. This study adds to current knowledge by suggesting that elevated aortic stiffness may contribute to the reduced ability of the cerebrovasculature to dilate in response to physiological stimuli but is not associated with age-related declines in global cerebral blood flow.

Summary

Age-related increases in aortic stiffness is associated with reduced cerebrovascular reserve, but not basal global cerebral blood flow, in older adults independent of age, sex, and blood pressure.

Higher Aortic Stiffness Is Associated With Lower Global Cerebrovascular Reserve Among Older Humans

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Hypertension. 2018;72:476-482; originally published online June 18, 2018;
doi: 10.1161/HYPERTENSIONAHA.118.11143
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0194-911X. Online ISSN: 1524-4563

ONLINE SUPPLEMENT

Higher Aortic Stiffness is Associated with Lower Cerebrovascular Reserve but not Global Cerebral Blood Flow Among Older Humans

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Table S1: Correlational matrix of adjusted cfPWV for delay between imaging and vascular visits and gCBF, absCVR and relCVR(%)

Variable	cfPWV	gCBF	absCVR	relCVR(%)
Adjusted cfPWV	0.99 (p<0.001)	0.08 (0.752)	-0.84 (<0.001)	-0.80 (<0.001)

Data are partial correlation coefficients (p values). cfPWV, carotid-femoral pulse wave velocity; gCBF, global cerebral blood flow; absCVR, absolute cerebrovascular reactivity; relCVR, relative (%) cerebrovascular reactivity.

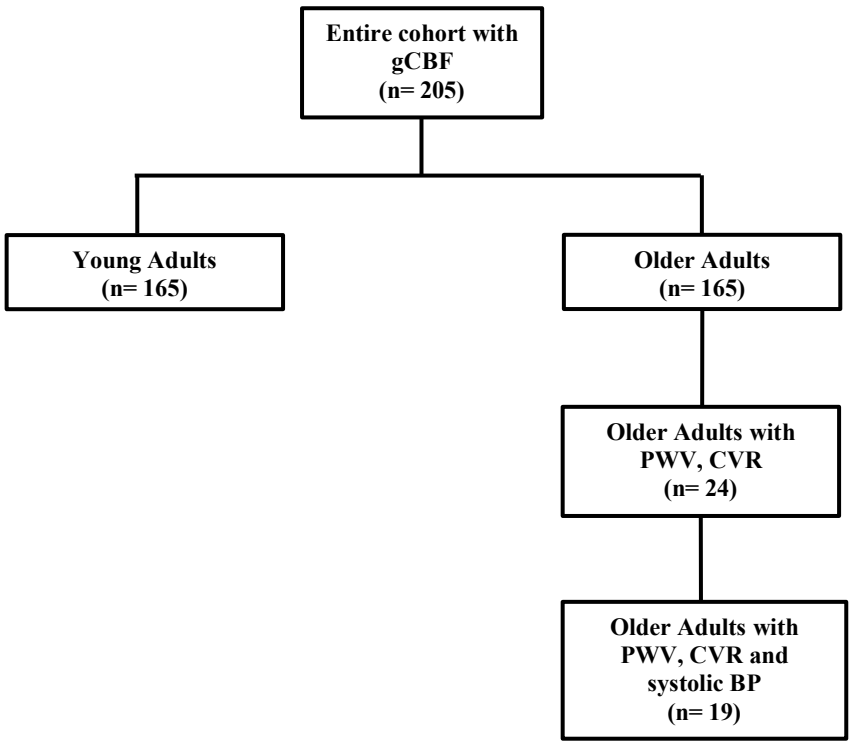

Figure S1. Description of subject groups in the entire cohort and subset analyses. Global cerebral blood flow, gCBF; pulse wave velocity, PWV; cerebrovascular reserve, CVR; blood pressure, BP.