Association Between Central Blood Pressure and Subclinical Cerebrovascular Disease in Older Adults

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See Editorial, pp 295–296

Abstract—Elevated blood pressure (BP) level is one of the most consistently identified risk factors for silent brain disease. BP values obtained at the proximal segment of the aorta (central BP) are more directly involved than brachial BP in the pathogenesis of cardiovascular disease. However, the association between central BP and silent cerebrovascular disease has not been clearly established. Participants in the CABL (Cardiovascular Abnormalities and Brain Lesions) study (n=993; mean age, 71.7±9.3 years; 37.9% men) underwent 2-dimensional echocardiography, arterial wave reflection analysis for determination of central BPs, and brain magnetic resonance imaging. Central BPs were calculated from the radial pulse waveform. Subclinical silent cerebrovascular disease was defined as silent brain infarction and white matter hyperintensity volume. Both brachial (P=0.014) and central pulse pressure (P=0.026) were independently associated with silent brain infarctions after adjustment for clinical variables, but not adjusting for each other. None of the brachial BP values was associated with upper quartile of white matter hyperintensity volume in multivariable analysis. Both central systolic BP (P<0.001) and central pulse pressure (P<0.001) were significantly associated with upper quartile of white matter hyperintensity volume in multivariable analysis, even after adjustment for brachial BP. In a predominantly older population-based cohort, both brachial and central pulse pressure were independently associated with silent brain infarction. However, higher central systolic BP and central pulse pressure, but not brachial BP, were significantly associated with white matter hyperintensity volume. **(*Hypertension*. 2020;75:580-587. DOI: 10.1161/HYPERTENSIONAHA.119.13478.)** ● **Online Data Supplement**

Key Words: brain infarction ■ cardiovascular diseases ■ hypertension ■ stroke ■ white matter

Silent brain infarcts (SBI) and white matter hyperintensities (WMHs) on magnetic resonance imaging (MRI) are frequently observed in older adults without apparent neurological symptoms.[1] SBI and WMH are associated with cognitive decline,[1] dementia,[2] and depression.[3] Moreover, both SBI and WMH are associated with increased risk of stroke.[1] Because of the significance of stroke as a leading cause of disability and the second-leading cause of death worldwide,[4] identifying individuals at increased risk of subclinical cerebrovascular disease may allow for earlier and more-effective stroke prevention strategies.

Hypertension is associated with a variety of cardiovascular diseases, including stroke, coronary artery disease, peripheral vascular disease, and heart failure.[5] Elevated blood pressure (BP) levels are one of the most consistently identified risk factors for SBI and WMH.[1,6,7] BP values obtained at the level of the proximal segment of the aorta (central BP) are more relevant than brachial BP for the pathogenesis of cardiovascular disease.[8–11] Moreover, the normal relationship between central BP and brachial BP is modified in older compared with younger adults because of the increasing arterial stiffness associated with aging.[8,9] Central BP can be easily and noninvasively derived from the arterial waveform obtained at the radial artery by applanation tonometry.[10] Previous studies demonstrated that central BP had a stronger association with cardiovascular events, including stroke, than brachial BP in community-based cohorts.[12–14] The association between central BP and silent cerebrovascular disease has not been clearly established, nor has a comparison between central BP and brachial BP been performed. The few studies on the topic have shown conflicting results and have been limited by small sample sizes[15–18] and relatively young age of participants.[15,16,19] Accordingly, the aim of the present study was to investigate the associations of central and brachial BP with subclinical cerebrovascular disease in a predominantly older population-based cohort without history of stroke.

Received May 30, 2019; first decision May 21, 2019; revision accepted October 15, 2019.

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The online-only Data Supplement is available with this article at https://www.ahajournals.org/doi/suppl/10.1161/HYPERTENSIONAHA.119.13478.

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Hypertension **is available at https://www.ahajournals.org/journal/hyp** **DOI: 10.1161/HYPERTENSIONAHA.119.13478**

Methods

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

Study Population

The study population was drawn from the CABL (Cardiovascular Abnormalities and Brain Lesions) study, which was designed to investigate the cardiovascular predictors of subclinical cerebrovascular disease in a community-based cohort. CABL based its recruitment on the NOMAS (Northern Manhattan Study), an observational, prospective, population-based cohort of stroke-free participants who enrolled from the Northern Manhattan neighborhood between 1993 and 2001. The details about the study design and recruitment of NOMAS have been described previously.[20] Between 2003 and 2008, all NOMAS participants remaining stroke-free were invited to participate in an MRI substudy. Subjects were eligible if older than 55 years and without contraindications to MRI. From September 2005, NOMAS MRI participants who voluntarily agreed to undergo a more extensive cardiovascular evaluation including echocardiographic parameters and central BPs were included in the CABL study. Thus, of the total of 1004 participants included in CABL, 993 who successfully underwent 2-dimensional echocardiography and applanation tonometry of the radial artery constituted the population of present study. Written informed consent was obtained from all study participants. The study was approved by the Institutional Review Boards of Columbia University Medical Center and the University of Miami.

Risk Factor Assessment and Brachial BP Measurement

Cardiovascular risk factors were ascertained through direct examination and interviews conducted by trained research assistants. Among the variables used in the analysis, hypertension was defined as brachial systolic BP (SBP) ≥140 mm Hg or diastolic BP (DBP) ≥90 mm Hg, or antihypertensive medication use. Hypercholesterolemia was defined as total serum cholesterol >240 mg/dL, or the use of lipid-lowering medications. Diabetes mellitus was defined by current use of insulin or hypoglycemic agents, or a fasting glucose of ≥126 mg/dL, tested on ≥2 occasions. Atrial fibrillation was defined from an ECG performed at the time of echocardiography or from self-reported history. Body mass index was calculated using height and weight (kilogram per square meter). Coronary artery disease was defined as a history of myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, typical angina, or use of anti-ischemic medications. Both brachial SBP and DBP were measured on the nondominant arm in a sitting position after 5 minutes of rest, using a mercury sphygmomanometer and with arm cuff of appropriate size. Brachial BPs were recorded twice with a 5-minute interval at the time of brain MRI, and the average of the 2 recordings was used. Brachial pulse pressure (PP) was defined as the difference between SBP and DBP.

Central BP Measurement

For determination of central BPs, pulse wave analysis of the radial artery by applanation tonometry was performed using a commercially available device (SphygmoCor, Pulse Wave Analysis System, AtCor Medical, Sydney, Australia). A detailed description of the technique and reproducibility data have been previously published.[21] Central SBP, DBP, and PP were calculated from the radial pulse wave by a validated generalized transfer function.[22]

Two-Dimensional Echocardiographic Examination

Transthoracic echocardiographic evaluation was performed according to a standardized protocol.[23] Detailed information about methods for the echocardiography was shown in the online-only Data Supplement.

Image Acquisition and Interpretation of Brain MRI

A detailed description of the assessment of subclinical cerebrovascular lesions has been previously published.[24,25] Briefly, imaging was performed on a 1.5-T MRI system (Philips Medical Systems, Andover, MA) at Columbia University Medical Center. SBIs were defined as either a cavitation on the fluid-attenuated inversion recovery sequence of at least 3 mm in size, distinct from a vessel (owing to the lack of signal void on T2 sequence), and of equal intensity to cerebrospinal fluid in the case of lacunar infarction, or as a wedge-shaped cortical or cerebellar area of encephalomalacia with surrounding gliosis consistent with infarction attributable to distal arterial branch occlusion. Interobserver agreement with regard to the detection of SBI was 93.3%.[25] WMH volume (WMHV) was determined in fluid attenuated inversion recovery images using the Quantum 6.2 package (Uetikon am See, Switzerland) on a Sun Microsystems Ultra 5 workstation. WMHV was expressed as the proportion of total cranial volume corrected for differences in head size. The upper quartile of WMHV (WMHV-Q4) was used as the dependent variable in the categorical analyses. All measurements were analyzed blinded to participant clinical information.

Statistical Analysis

Continuous data are presented as mean±SD, and categorical variables are expressed as frequencies and percentages. Univariable and multivariable logistic regression analyses were used to evaluate the associations between both brachial and central BP measurements and subclinical cerebrovascular disease. Independent predictors of SBI or upper quartile of WMHV were identified by entering all variables associated with a probability value 0.05 or less in the univariable analysis and the time interval between cardiovascular evaluation and MRI into a multivariable logistic regression analysis. Odds ratios and 95% CIs for significant independent variables in the multivariable analysis were calculated. All calculations were performed using SAS version 9.3 (SAS Institute, Cary, NC), and P <0.05 were considered statistically significant.

Results

Study Population

Table 1 shows the baseline characteristics of the study cohort. The mean age of the study population was 71.7±9.3 years and 37.9% of participants were men. Among 793 (79.9%) participants with hypertension at baseline, 723 (72.8%) reported use of antihypertensive drugs. Mean brachial BP was 135.9/78.2 mm Hg. For central BP measurements, mean central SBP, DBP, and PP were 120.3, 71.7, and 48.6 mm Hg, respectively. SBI was present in 144 cases (14.5%). Mean WMHV was 0.64±0.81% (median, 0.34%, interquartile range=0.52%).

Clinical Variables and Silent Cerebrovascular Disease

Clinical variables associated with SBI and upper quartile of WMHV using univariable logistic regression analysis are shown in Table 2. Older age (P<0.001), presence of hypertension (P=0.002) and atrial fibrillation (P=0.001), lower left ventricular (LV) ejection fraction (P=0.021), higher LV mass index (P<0.001) and greater left atrial diameter index (P<0.001) were significantly associated with the presence of SBI. Male sex showed a marginal association with SBI (P=0.052). Older age (P<0.001), black race/ethnicity (P=0.002), presence of hypertension (P<0.001) and atrial fibrillation (P=0.005), lower body mass index (P=0.004), higher heart rate (P=0.013), greater LV mass index (P<0.001), and higher left atrial diameter index (P<0.001) were significantly associated with the upper quartile of WMHV.

Brachial BP, Central BP, and SBI

Univariable and multivariable logistic regression were performed to identify BP variables associated with SBI (Table 3).

Table 1. Baseline Characteristics of the Study Population

Characteristic	n=993
Age, y	71.7±9.3
Male sex, n (%)	376 (37.9%)
Race	
White, n (%)	140 (14.1%)
Black, n (%	157 (15.8%)
Hispanic, n (%)	674 (67.9%)
Others, n (%)	22 (2.2%)
Hypertension, n (%)	793 (79.9%)
Antihypertensive drug use, n (%)	723 (72.8%)
Hypercholesterolemia, n (%)	674 (67.9%)
Statin use, n (%)	500 (50.4%)
Diabetes mellitus, n (%)	294 (29.6%)
Smoking history, n (%)	524 (52.8%)
Atrial fibrillation, n (%)	62 (6.2%)
BMI, kg/m^2	28.3±4.9
Underweight (BMI<18.5), n (%)	8 (0.8%)
Normal weight (18.5≤BMI<25), n (%)	249 (25.1%)
Overweight (BMI≥25), n (%)	736 (74.1%)
Coronary artery disease, n (%)	60 (6.0%)
Heart rate, bpm	67.9±11.1
Brachial BP variables	
Brachial SBP, mm Hg	135.9±17.5
Brachial DBP, mm Hg	78.2±9.6
Brachial PP, mm Hg	57.7±14.9
Central BP variables	
Central SBP, mm Hg	120.3±19.0
Central DBP, mm Hg	71.7±10.3
Central PP, mm Hg	48.6±15.7
Echocardiographic variables	
LV ejection fraction, %	63.7±7.1
LV ejection fraction <50%, n (%)	41 (4.1%)
LV ejection fraction <35%, n (%)	8 (0.8%)
LV mass index, g/m^2	103.0±26.1
LA diameter index, mm/m^2	22.4±3.2
Brain MRI	
SBI, n (%)	144 (14.5%)
WMHV/total cranial volume, %	0.64±0.81

Values are mean±SD or n (%). BMI indicates body mass index; BP, blood pressure; DBP, diastolic blood pressure; LA, left atrial; LV, left ventricle; MRI, magnetic resonance imaging; PP, pulse pressure; SBI, silent brain infarcts; SBP, systolic blood pressure; and WMHV, white matter hyperintensity volume.

Among brachial BP measurements, SBP and PP were associated with SBI (both $P<0.01$), whereas brachial DBP did not show a significant association with SBI in the univariable analysis. On the contrary, lower central DBP and higher central PP were directly associated with SBI in unadjusted models (both $P<0.05$). In the multivariable analysis with adjustment for age, sex, hypertension, atrial fibrillation, and time interval between tests, both brachial and central PP were independently associated with SBI (both $P<0.05$). Furthermore, an additional model to assess whether central BPs are associated with SBI independently from brachial BPs was performed by entering both pressures in the same model (Table 4). No central BP measurements show significant relationships with SBI after adjustment for brachial BP.

When hypertension was defined as brachial SBP ≥130 mm Hg or DBP ≥80 mm Hg, or antihypertensive medication use in accordance with the most recent guidelines,[26] these significant associations remained consistent (Table S1 in the online-only Data Supplement). However, these associations did not reach statistical significance after further adjustment for pertinent echocardiographic variables (Table S2).

Because 22 of 144 SBIs (15.3%) were cortical lesions, which may have nonmicrovascular origin and might have diluted the association between BP values and SBI, we performed a sensitivity analysis excluding those cortical lesions; even in this analysis, central SBP ($P=0.45$), central PP ($P=0.50$), brachial SBP ($P=0.35$), and brachial PP ($P=0.21$) were not associated with SBI in multivariable models.

Brachial BP, Central BP, and Upper Quartile of WMHV

The association between BP variables and the upper quartile of WMHV is shown in Table 5. Although brachial SBP and PP were associated with WMHV-Q4 in univariable analysis (both $P<0.001$), no significant association persisted in multivariable analysis. Central SBP and central PP were significantly associated with the upper quartile of WMHV in unadjusted models (both $P<0.001$). These associations persisted after adjustments for possible clinical confounders ($P<0.001$). Both central SBP and central PP were still associated with WMHV-Q4 after further adjustment for brachial BP (Table 6).

Moreover, central SBP and PP remained independently associated with the presence of WMHV-Q4 even after applying the lower BP cutoffs (130/80 mm Hg) from the current hypertension guidelines (Table S1), and after further adjustment for echocardiographic variables (Table S2).

Discussion

In our community-based population free of stroke, we demonstrate that a significant relationship exists between central BP and silent cerebrovascular disease. Both brachial and central BP measurements were associated with subclinical disease in univariable analyses. Although brachial and central BP showed similar lack of a significant association with SBI in multivariable analyses, central BP, but not brachial BP, was independently associated with the presence of upper quartile of WMH after adjustment for possible confounders.

Central SBP and PP for the Prediction of Cardiovascular Disease

Central BP has been shown to have better predictive value for cardiovascular outcomes, including brain disease, than brachial BP. As central BP provides an accurate representation

Table 2. Clinical Variables Associated With Silent Brain Infarction and Upper Quartile of White Matter Hyperintensity Volume

	SBI		WMHV-Q4	
Variable	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age, >70 y	2.49 (1.68–3.69)	<0.001	5.25 (3.67–7.49)	<0.001
Sex, male	1.42 (1.00–2.03)	0.052	0.89 (0.66–1.19)	0.43
Race				
White	1 (reference)		1 (reference)	
Black	1.43 (0.79–2.59)	0.24	2.24 (1.33–3.78)	0.002
Hispanic	0.76 (0.46–1.27)	0.30	1.13 (0.73–1.77)	0.58
Others	1.58 (0.53–4.72)	0.42	2.19 (0.84–5.71)	0.11
Hypertension	2.40 (1.37–4.19)	0.002	2.76 (1.76–4.31)	<0.001
Hypercholesterolemia	1.01 (0.69–1.48)	0.96	0.91 (0.67–1.23)	0.53
Statin use	1.16 (0.81–1.65)	0.42	1.04 (0.78–1.38)	0.81
Diabetes mellitus	1.27 (0.87–1.85)	0.21	1.12 (0.82–1.52)	0.49
Smoking history	1.03 (0.73–1.47)	0.86	1.15 (0.86–1.54)	0.33
Atrial fibrillation	2.61 (1.46–4.67)	0.001	2.13 (1.26–3.62)	0.005
BMI, kg/m^2	0.98 (0.94–1.01)	0.20	0.96 (0.93–0.99)	0.004
Underweight (BMI<18.5)	0.68 (0.08–5.71)	0.73	1.37 (0.32–5.86)	0.67
Normal weight (18.5≤BMI<25)	1 (reference)		1 (reference)	
Overweight (BMI≥25)	0.75 (0.51–1.11)	0.15	0.68 (0.50–0.94)	0.020
Coronary artery disease	1.69 (0.89–3.22)	0.11	1.54 (0.88–2.68)	0.13
Heart rate, per 10 bpm	1.04 (0.89–1.21)	0.65	1.17 (1.03–1.32)	0.013
Echocardiography				
LV ejection fraction, %	0.97 (0.95–1.00)	0.021	0.99 (0.97–1.01)	0.19
LV mass index, g/m^2	1.02 (1.01–1.02)	<0.001	1.02 (1.01–1.02)	<0.001
LA diameter index, mm/m^2	1.10 (1.04–1.16)	<0.001	1.11 (1.06–1.16)	<0.001

Univariable logistic regression analysis. BMI indicates body mass index; LA, left atrial; LV, left ventricle; OR, odds ratio; SBI, silent brain infarcts; and WMHV-Q4, upper quartile of white matter hyperintensity volume.

of perfusion pressure of the cerebral vessels, it is conceivable that central BP may affect the likelihood to develop preclinical cerebrovascular diseases.[8,9,11] Among the central BP variables, our study showed that SBP and PP, as indicators of pulsatile pressure, were more strongly associated with silent cerebrovascular diseases than corresponding brachial BPs. This finding is consistent with the excellent predictive value of central SBP and PP for cardiovascular outcomes reported in previous studies. Pini et al[12] demonstrated that central SBP and PP, but not brachial SBP or PP, independently predicted

Table 3. Blood Pressure Variables Associated With Silent Brain Infarction

	Univariable		Multivariable Model*	
BP Variable	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Brachial BP variables				
Brachial SBP, per 10 mm Hg	1.17 (1.06–1.29)	0.002	1.11 (1.00–1.24)	0.058
Brachial DBP, per 10 mm Hg	0.97 (0.80–1.16)	0.73	0.95 (0.79–1.15)	0.62
Brachial PP, per 10 mm Hg	1.26 (1.12–1.41)	<0.001	1.17 (1.03–1.33)	0.014
Central BP variables				
Central SBP, per 10 mm Hg	1.08 (0.99–1.18)	0.095	1.04 (0.95–1.15)	0.42
Central DBP, per 10 mm Hg	0.80 (0.67–0.95)	0.012	0.85 (0.71–1.02)	0.082
Central PP, per 10 mm Hg	1.22 (1.09–1.35)	<0.001	1.14 (1.02–1.29)	0.026

Univariable and multivariable logistic regression analysis. BP indicates blood pressure; DBP, diastolic blood pressure; OR, odds ratio; PP, pulse pressure; and SBP, systolic blood pressure.

*Adjusted for age, sex, hypertension, atrial fibrillation, and time interval between tests.

Table 4. Comparison of the Association of Brachial and Central Blood Pressure With Silent Brain Infarction

	Multivariable Model 1*		Multivariable Model 2†	
Brachial vs Central BP	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Brachial vs central SBP				
Brachial SBP, per 10 mm Hg	1.16 (1.04–1.30)	0.007	1.11 (0.99–1.25)	0.086
Central SBP, per 10 mm Hg	1.02 (0.92–1.12)	0.77	1.01 (0.91–1.12)	0.90
Brachial vs central DBP				
Brachial DBP, per 10 mm Hg	1.11 (0.90–1.36)	0.34	1.05 (0.84–1.31)	0.67
Central DBP, per 10 mm Hg	0.76 (0.62–0.93)	0.008	0.83 (0.67–1.03)	0.084
Brachial vs central PP				
Brachial PP, per 10 mm Hg	1.18 (1.04–1.34)	0.011	1.13(0.99–1.29)	0.073
Central PP, per 10 mm Hg	1.14 (1.01–1.28)	0.040	1.10 (0.97–1.25)	0.15

BP indicates blood pressure; DBP, diastolic blood pressure; OR, odds ratio; PP, pulse pressure; and SBP, systolic blood pressure.

*Brachial and central blood pressure are included in the same model.

†Brachial and central blood pressure are included in the same model adjusted for age, sex, hypertension, atrial fibrillation, and time interval between tests.

future cardiovascular events in the Dicomano Study. Similarly, central PP was more strongly associated with future cardiovascular events than brachial BP in the Strong Heart study.[14] Furthermore, a recent meta-analysis suggested that central PP may be a better predictor for future events than brachial PP although it did not reach independent statistical significance in multivariate analysis (P=0.057).[11] For cerebrovascular disease, Chuang et al[13] recently demonstrated that central SBP is a significant predictor for future stroke. Increased pulsatility, which is correlated with higher central SBP and PP,[13] may directly and negatively impact cerebral vessel integrity, particularly in watershed areas of cerebral circulation. This possible underlying mechanism of stroke and silent brain disease[6,7,9,15] may also provide a possible explanation for our results.

Central BP and SBI

In the present study, the relationship of central BP with SBI was weaker than that with WMH. Both brachial and central PP were independently associated with SBI in multivariable analysis. As PP rises with age, particularly after 60 years,[7] elevated PPs may be strong indicators of high pulsatility in our older population. In fact, this result is consistent with previous studies in older cohorts.[6,18] On the contrary, Ochi et al[15] showed a significant association between central SBP and SBI in the Japanese population but also a relationship between both SBPs and SBI that we did not confirm. The high frequency of antihypertensive use in our cohort, and the lower mean SBP (by ≈10 mm Hg compared with the Japanese cohort) may have affected our ability to detect an independent role for SBP. Furthermore, we adjusted for cardiac variables, such as LV mass[27] and left atrial size,[28] both associated with elevated BP and silent brain disease. This further adjustment may have been a factor in weakening the association that we observed between central BP and SBI. On the contrary, central PP was not significantly associated with silent cerebral disease in the Framingham Offspring study.[19] Compared with the CABL participants, the relatively better baseline health status of the Framingham cohort may have weakened the ability to detect the association between central BP and silent brain disease.

Moreover, we found central PP to be no longer associated with SBI after adjustment for brachial BP. The significant

Table 5. Clinical Variables Associated With Upper Quartile of White Matter Hyperintensity Volume

	Univariable		Multivariable Model*	
BP Variable	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Brachial BP variables				
Brachial SBP, per 10 mm Hg	1.17 (1.08–1.27)	<0.001	1.08 (0.98–1.19)	0.15
Brachial DBP, per 10 mm Hg	1.08 (0.93–1.26)	0.30	1.13 (0.96–1.34)	0.15
Brachial PP, per 10 mm Hg	1.21 (1.10–1.33)	<0.001	1.04 (0.93–1.16)	0.50
Central BP variables				
Central SBP, per 10 mm Hg	1.21 (1.12–1.30)	<0.001	1.19 (1.09–1.29)	<0.001
Central DBP, per 10 mm Hg	0.93 (0.80–1.07)	0.28	1.09 (0.94–1.28)	0.25
Central PP, per 10 mm Hg	1.37 (1.25–1.51)	<0.001	1.27 (1.14–1.42)	<0.001

Univariable and multivariable logistic regression analysis. BP indicates blood pressure; DBP, diastolic blood pressure; OR, odds ratio; PP, pulse pressure; and SBP, systolic blood pressure.

*Adjusted for age, race, hypertension, atrial fibrillation, body mass index, heart rate, and time interval between tests.

Table 6. Comparison of the Association of Brachial and Central Blood Pressure With Upper Quartile of White Matter Hyperintensity Volume

	Multivariable Model 1*		Multivariable Model 2†	
Brachial vs Central BP	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Brachial vs central SBP				
Brachial SBP, per 10 mm Hg	1.09 (0.99–1.19)	0.067	1.01 (0.91–1.12)	0.92
Central SBP, per 10 mm Hg	1.17 (1.08–1.27)	<0.001	1.18 (1.08–1.30)	<0.001
Brachial vs central DBP				
Brachial DBP, per 10 mm Hg	1.17 (0.98–1.38)	0.076	1.11 (0.92–1.34)	0.30
Central DBP, per 10 mm Hg	0.87 (0.74–1.01)	0.074	1.05 (0.88–1.25)	0.60
Brachial vs central PP				
Brachial PP, per 10 mm Hg	1.05 (0.94–1.17)	0.43	0.95 (0.84–1.07)	0.41
Central PP, per 10 mm Hg	1.35 (1.22–1.50)	<0.001	1.29 (1.15–1.45)	<0.001

BP indicates blood pressure; DBP, diastolic blood pressure; OR, odds ratio; PP, pulse pressure; and SBP, systolic blood pressure.

*Brachial and central blood pressure are included in the same model.

†Brachial and central blood pressure are included in the same model adjusted for age, race, hypertension, atrial fibrillation, body mass index, heart rate, and time interval between tests.

correlation between brachial and central BPs may have been a factor in weakening the association that we observed between them and SBI.

As the definition of SBI in this study, which included cortical lesions that may recognize a nonmicrovascular etiology, might dilute the strength of their associations with the vascular risk factors, we further analyzed the association between BP variables and SBI excluding the cortical lesions. However, neither central SBP nor central PP (or the corresponding brachial values) showed a significant association with SBI in the in fully adjusted models of this sensitivity analysis, suggesting that the lack of association was not driven by heterogeneity in the lesions considered as SBI.

Surprisingly, we did not observe a significant association between diabetes mellitus and the presence of silent cerebrovascular disease. However, despite the well-established role of diabetes mellitus as a risk factor for vascular diseases including stroke, recent systematic reviews showed that the association between diabetes mellitus and silent brain disease remains unclear.[29]

Central BP and WMH

Higher central SBP and PP were significantly associated with WMHV in multivariable analysis, even after adjustment for brachial BP, and even after further adjustment for pertinent echocardiographic parameters. These findings are consistent with a previous study that reported that central SBP was associated with WMHV, and this association was independent of atherosclerotic parameters including carotid artery intima-media thickness.[16] Although the pathophysiology of WMH remains uncertain and may be multifactorial, WMH is believed to be of at least partial vascular origin, representing areas of demyelination, gliosis, arteriosclerosis, and microinfarction presumed to be caused by ischemia.[1] These mechanisms may reflect the fact that the most consistently identified risk factors for WMH are advanced age and hypertension.[1] This may also explain why central SBP and central PP showed a stronger association with WMHV than with SBI in our study.

Strengths and Limitations

The main strength of the present study is the large population-based sample of predominantly older participants, and the extensive adjustment for possible confounders, including pertinent cardiac variables such as LV mass and left atrial size. However, our study also has several limitations. First, the study participants were older than 55 years and with a large representation of Hispanic ethnicity, which might not allow the extension of the results to populations with different demographics. Second, the frequency of hypertension and antihypertensive drug use in our cohort is relatively high. Although the significant associations between central BP and silent brain diseases persisted even after adjustment for antihypertensive treatment, the results might not be directly applicable to cohorts with different risk factors profiles or higher frequencies of normotensive subjects. Third, detailed information about the neurological diseases and baseline cognitive function was not included in the present study; although participants with prior stroke were excluded, participants with history of transient ischemic attacks were present in the CABL cohort. Finally, our results were derived from a cross-sectional design, which prevents establishing a causal relationship between central BP and silent cerebrovascular disease.

Perspectives

This study identified that both brachial and central PP were independently associated with SBI, whereas higher central SBP and PP, but not brachial BP, were significantly associated with WMHV in a predominantly older population-based cohort without history of stroke. Central BP, estimated noninvasively by radial applanation tonometry, has the potential to be clinically useful as an indicator subclinical brain damage from high BP.[8–11] Therefore, the measurement of central BP and consequent estimation of the risk of subclinical brain disease may be important for implementing more effective stroke prevention strategies. This possibility could be evaluated in future prospective studies. Moreover, antihypertensive drugs such as renin-angiotensin antagonists and calcium antagonists

may exert a greater effect on central BP than β blockers and diuretics despite similar effects on brachial BP.[8,10,30] Whether a differential effect of antihypertensive drugs on central BP may have different effects on cerebrovascular outcomes is a possibility that will require further investigation.

Sources of Funding

This work was supported by grants from the National Institute of Neurological Disorders and Stroke (grant R01 NS36286 to M.R. Di Tullio and R37 NS29993 to R.L. Sacco and M.S.V. Elkind).

Disclosures

None.

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Novelty and Significance

What Is New?

- The association between central blood pressure (BP) and silent cerebrovascular disease has not been clearly established nor has a comparison between central BP and brachial BP been performed.
- This study sought to investigate the associations of central BP and brachial BP with subclinical cerebrovascular disease in a predominantly older population-based large cohort.

What Is Relevant?

- Elevated BP level is one of the most consistently identified risk factors for silent brain disease.
- Our findings support the hypothesis that central BPs are more directly involved than brachial BP in the pathogenesis of cardiovascular disease.

Summary

Central systolic BP and central pulse pressure, but not brachial BP, were independently associated with the presence of silent cerebrovascular disease in a predominantly older population-based cohort.