Relationship Between Pulse Pressure, Arterial Stiffness and Cerebral Small Vessel Disease

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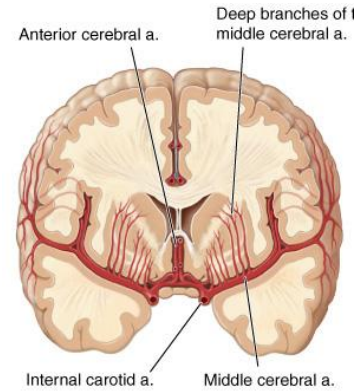
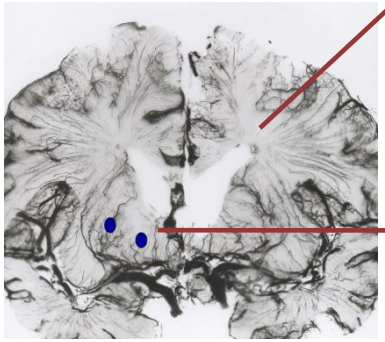
Contents

- Components of cerebral small vessel disease
- Pulse pressure and cerebral small vessel disease
- Treatment of cerebral small vessel disease

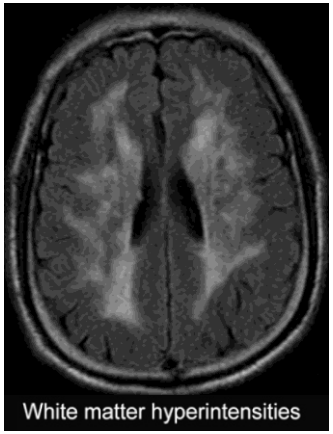
Expressions of cerebral small vessel disease

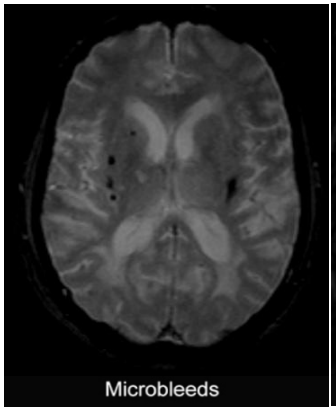
Cerebral small vessel

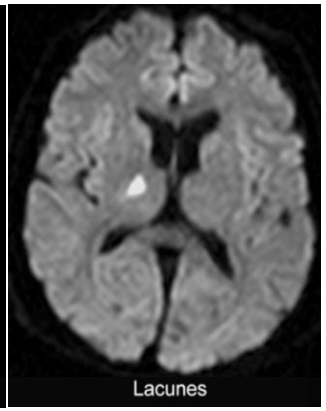




MR findings of CSVD







Clinical symptoms

Lacunar SD

Vascular dementia

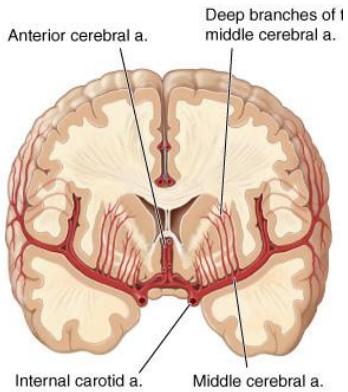
Gait disturbance

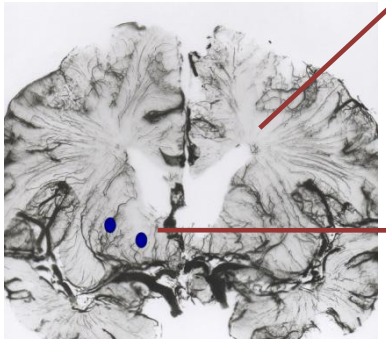
Depression

J Neurol Neurosurg Psychiatry 2011;82:126

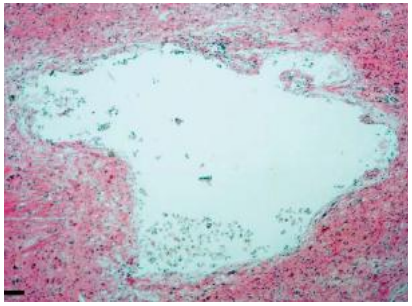
Pathology of cerebral small vessel disease

Cerebral small vessel

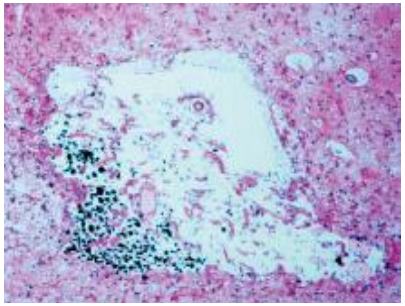




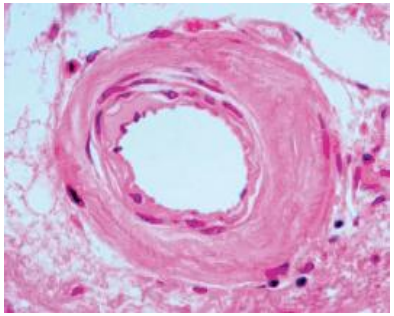
Pathologic findings



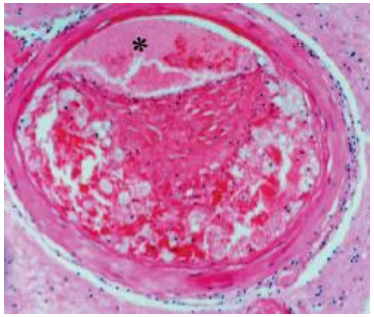
Complete lacune infarct



Small hemorrhage

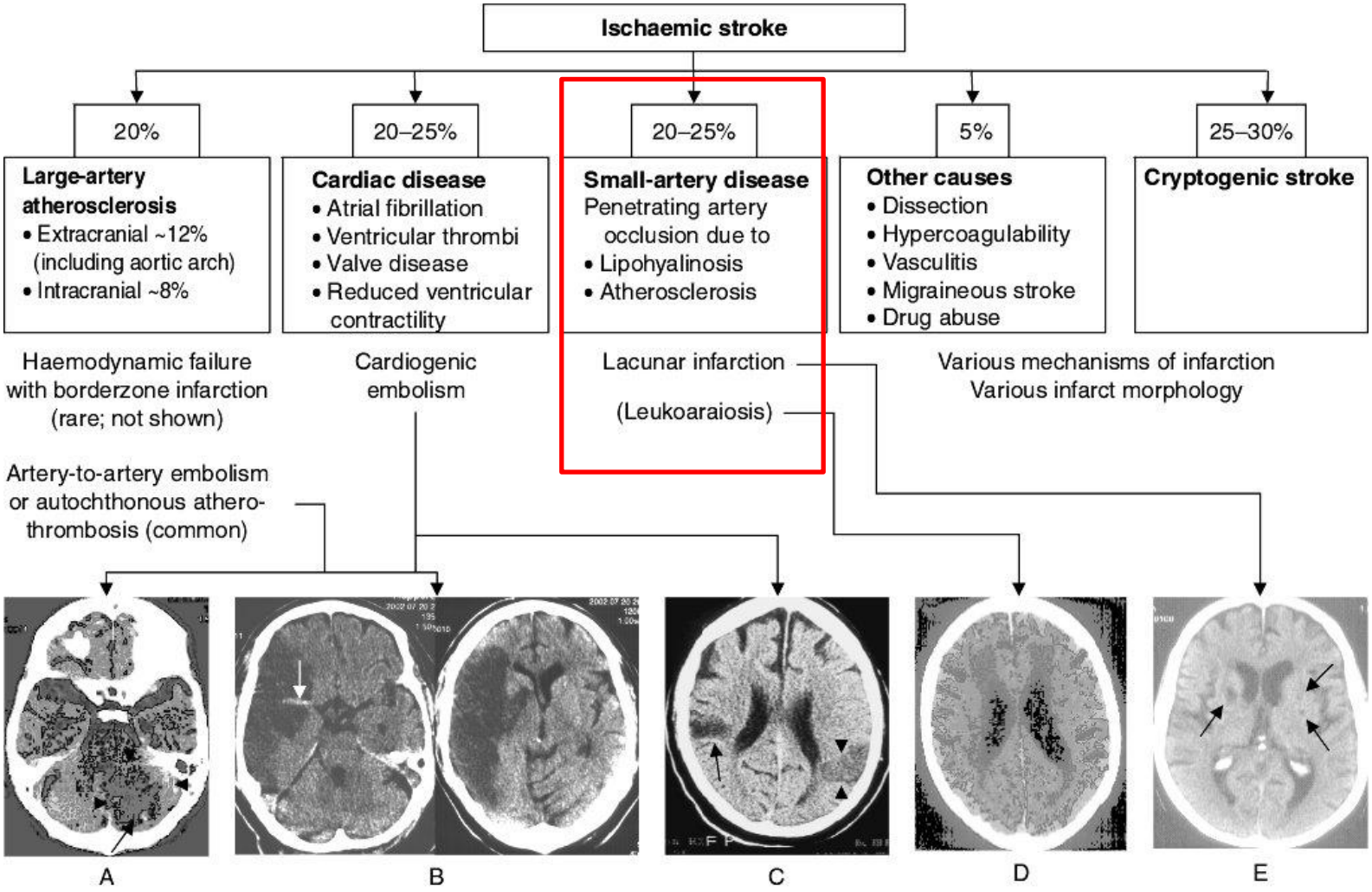


Hyaline arteriosclerosis

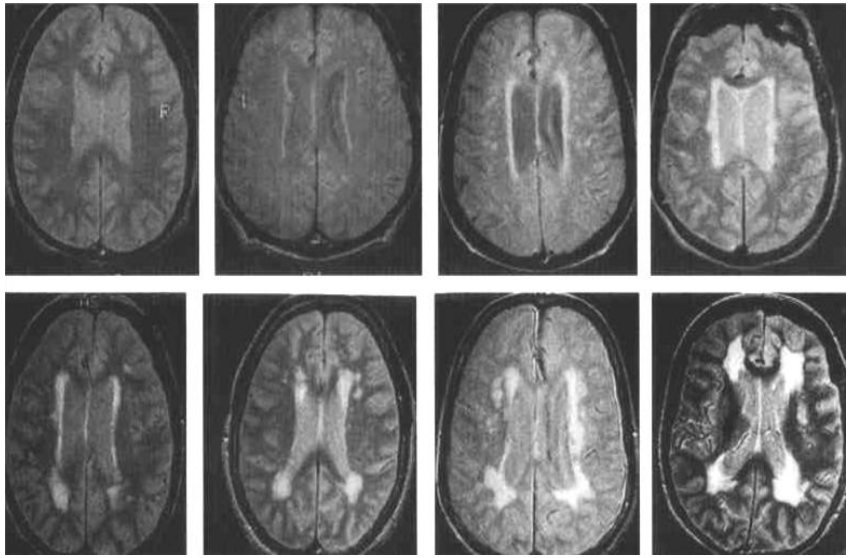


Eccentric atherosclerotic Plaque

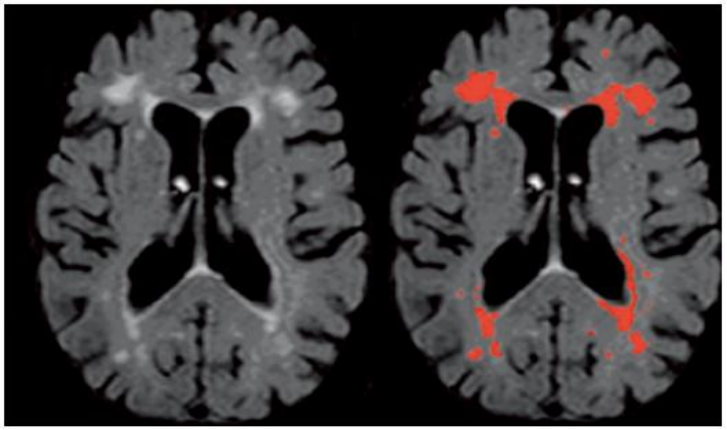
Comparison of Stroke Subtype



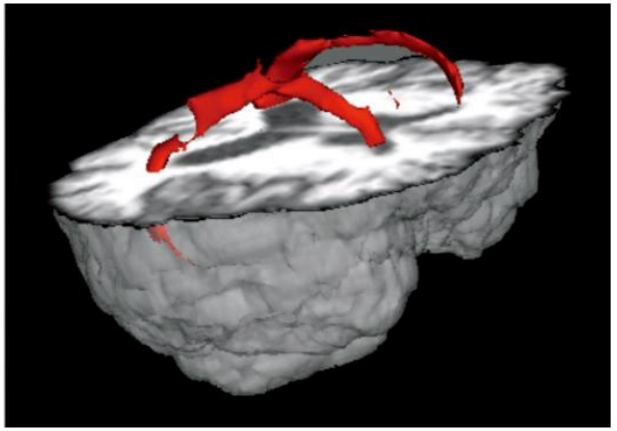
Quantification of white matter lesion



Cardiovascular Health study



WMHs on T2-weighted FLAIR raw image (left) and labeled with an intensity threshold (right)



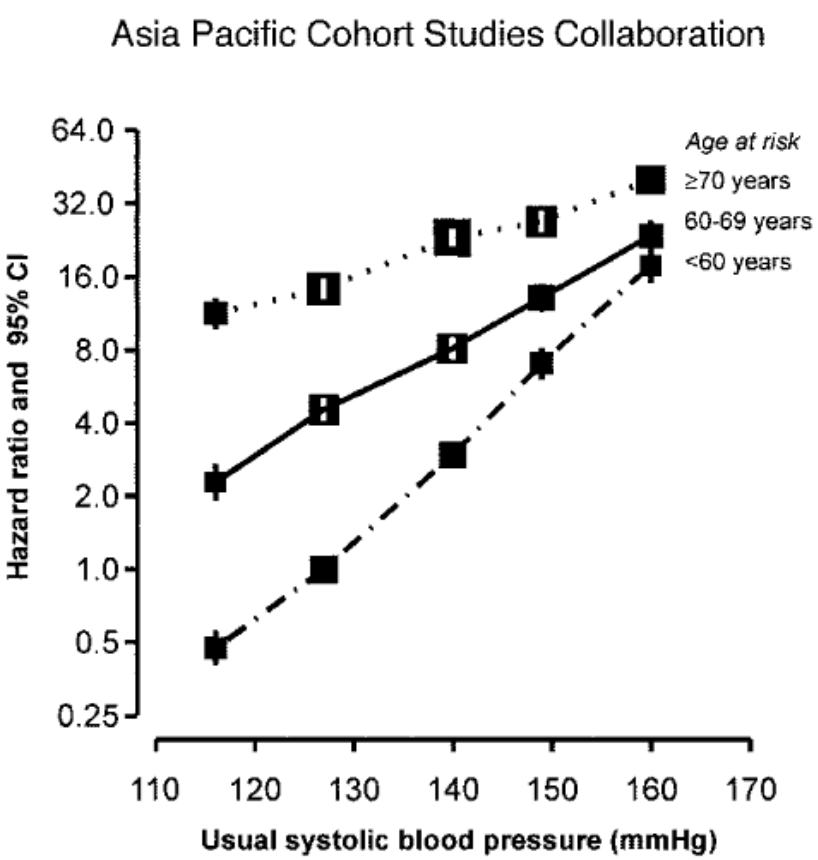
Three-dimensional reconstruction of WMHs

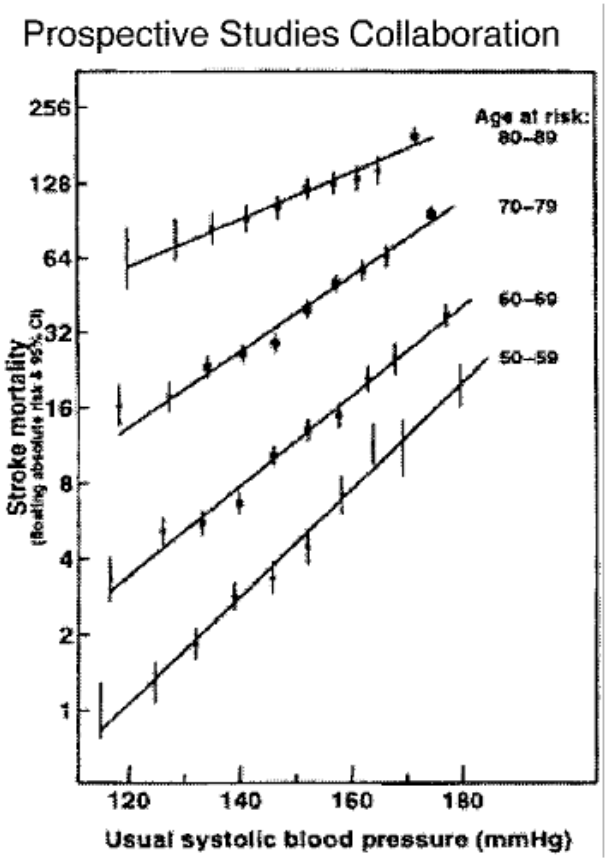
Characteristics of WMHs

- WMH are a surrogate marker of small-vessel vascular disease resulting from ischemic damage due to chronic hypoperfusion
- WMH were associated with chronological age and vascular risk factors
- Most severe among adults with the highest absolute blood pressure and blood pressure fluctuation over a 3-year period
- Stroke risk increased 3.5-fold, dementia risk increased 2-fold
- Death risk increased 2-fold

Contents

Associations between SBP and risk of stroke





Stroke 2004;35:1024

Pulse pressure and risk of stroke & WMLs

Stroke

TABLE 2. Risk Ratios for Factors Examined

Factor	Risk Ratio (95% Confidence Interval)	
	Stroke	Death
Pulse pressure (per 10 mm Hg increase)	1.11 (1.01–1.22), P=0.028	1.16 (1.08–1.24), P<0.001
MAP (per 10 mm Hg increase)	1.20 (1.02–1.42), P=0.031	1.14 (1.01–1.29), P=0.035
Age	1.63 (1.35–1.99), P<0.001	1.07 (1.06–1.09), P<0.001
HDL cholesterol (per 0.39-mmol/L increase)	0.86 (0.78–0.94), P<0.001	0.91 (0.84–0.98)
History of stroke	2.34 (1.15–4.78), P=0.019	
History of myocardial infarction	0.52 (0.26–1.07), P=0.075	
Current smoking	1.71 (1.22–2.39), P=0.002	2.13 (1.67–2.73), P<0.001
History of diabetes	2.02 (1.45–2.82), P<0.001	1.83 (1.40–2.38), P<0.001
Randomization (active)	0.67 (0.52–0.87), P=0.002	0.84 (0.69–1.02), P=0.079
ECG abnormality	1.46 (1.10–1.94), P=0.008	
Heart rate (per 10 bpm increase)	1.11 (0.99–1.25), P=0.087	1.02 (1.01–1.03), P<0.001
Race (nonblack)		0.78 (0.60–1.01), P=0.058
Gender (men)		1.58 (1.29–1.94), P<0.001

White matter lesions

Table 2 Association of advanced white matter lesions with quartiles of pulse pressure

Quartiles of PP (mmHg)	Advanced WMLs (grade 3 or higher)		
	Prevalence [*n* (%)]	OR (95% CI)	
		Age, sex, HT-adjusted[a]	Multivariable-adjusted[b]
≤37	10 (5.7)	Reference	Reference
38–44	13 (7.2)	1.04 (0.43–2.51)	1.06 (0.44–2.56)
45–53	18 (10.6)	1.33 (0.57–3.07)	1.29 (0.54–3.08)
≥54	55 (32.9)	2.81 (1.27–6.23)	2.55 (1.03–6.30)

CI, confidence interval; HT, hypertension; OR, odds ratio; PP, pulse pressure; WMLs, white matter lesions. [a] Odds ratio (95% CI) of cerebral WMLs, adjusted for age, sex and hypertension. [b] Additional adjustment for high systolic and diastolic blood pressure, aspirin use, the high level of high-sensitivity C-reactive protein, and cardiovascular risk factors (diabetes, ever smoking, coronary artery disease, the high levels of total cholesterol and triglyceride, and the low level of high-density lipoprotein cholesterol).

Hypertension 1999;34:375-380

J of hypertension 2011;29:325-329

Neuroepidemiology 1997;16:149-162

Arterial Stiffness and Stroke

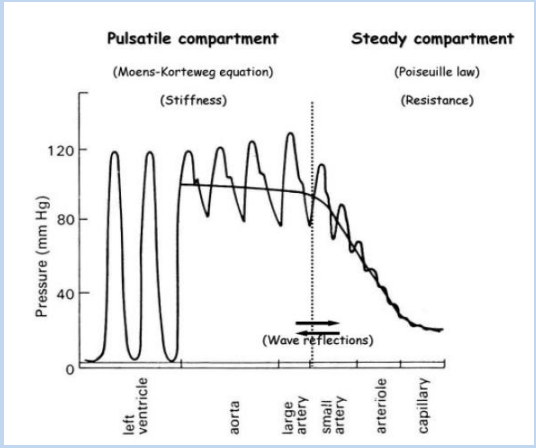
- Aortic stiffness is associated with ischemic stroke, independent of thickness of aortic arch plaques and other the risk of ischemic stroke in the elderly *Stroke* 2002;33:2077

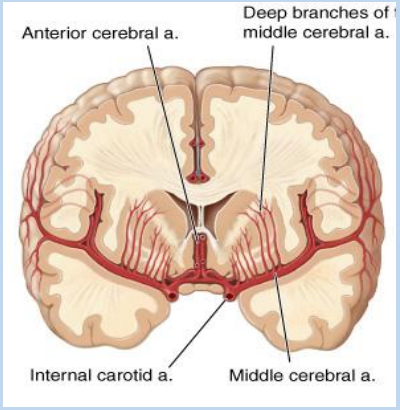
- In longitudinal study, aortic stiffness is an independent predictor of fatal stroke in patients with essential HT *Stroke* 2003;34:1203

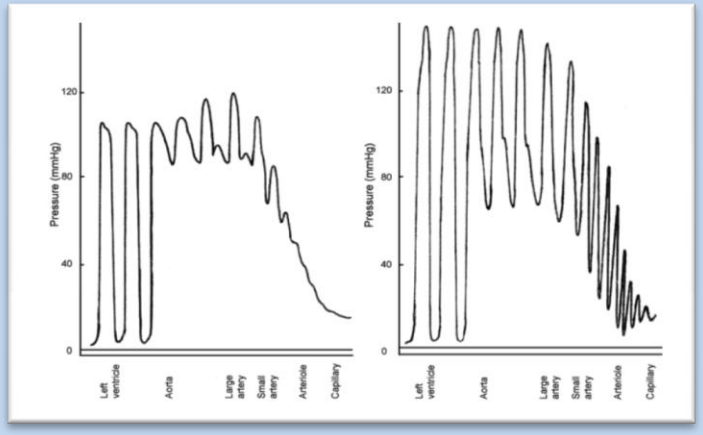
- The causal interrelationship between the elastic properties of the common carotid artery and the risk of stroke

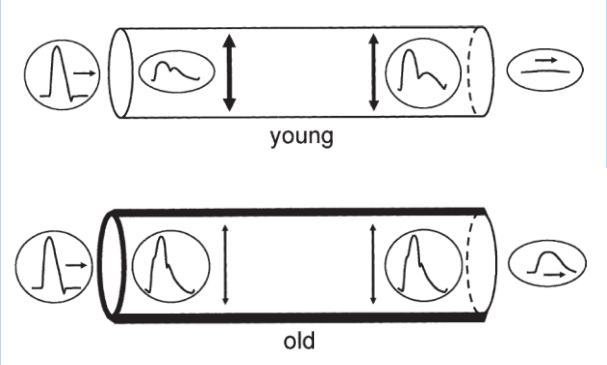
European J Neurol 2006;13:475

Pulsatile pressure changes in the vascular tree









How HT contributes to WM lesion?

Hypertension

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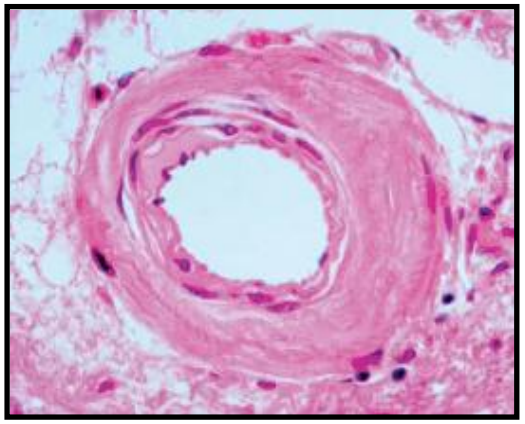
Structural changes of the arterioles in the brain
(hyalinization, tortuosity, elongation and narrowing)

↓

A decrease in blood flow and ischemia



Upwards shift of limits in the hypertensive

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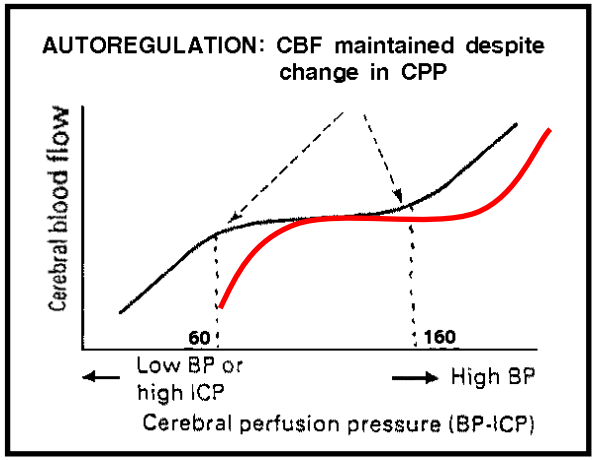
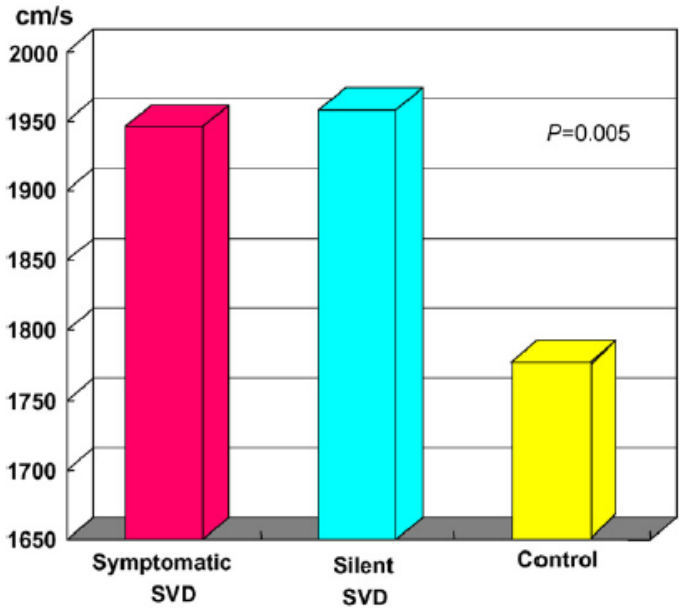
Transient falls in CBF
during periods of lower BP

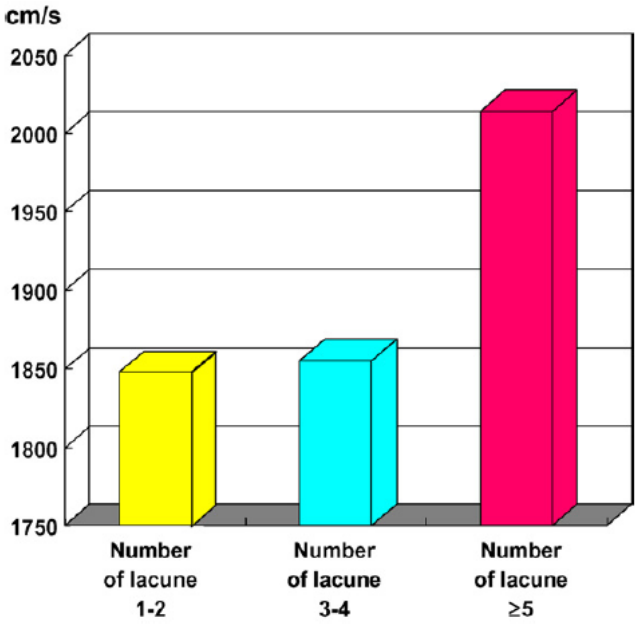


Arterial stiffness and cerebral small vessel disease

Increased brachial–ankle pulse wave velocity is independently associated with risk of cerebral ischemic small vessel disease in elderly hypertensive patients

Dae-Hyun Kim, Jei Kim, Jae-Moon Kim, Ae Young Lee*



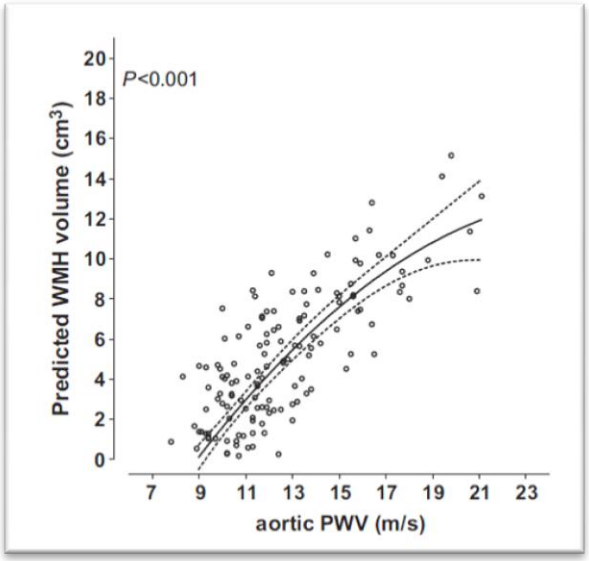


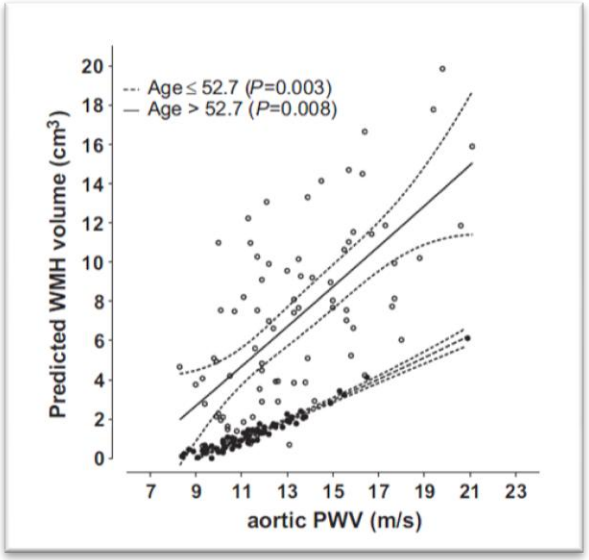
Clinical Neurology and Neurosurgery 2008;110:599

Arterial stiffness and cerebral small vessel disease

Increased Aortic Pulse Wave Velocity Is Associated With Silent Cerebral Small-Vessel Disease in Hypertensive Patients

Léon H.G. Henskens, Abraham A. Kroon, Robert J. van Oostenbrugge, Ed H.B.M. Gronenschild, Monique M.J.J. Fuss-Lejeune, Paul A.M. Hofman, Jan Lodder, Peter W. de Leeuw





Hypertension 2008;52::1120

Relationship between PWV and Cerebral SVD

Increased Aortic Pulse Wave Velocity Is Associated With Silent Cerebral Small-Vessel Disease in Hypertensive Patients

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(*Hypertension*. 2008;52:1120-1126.)

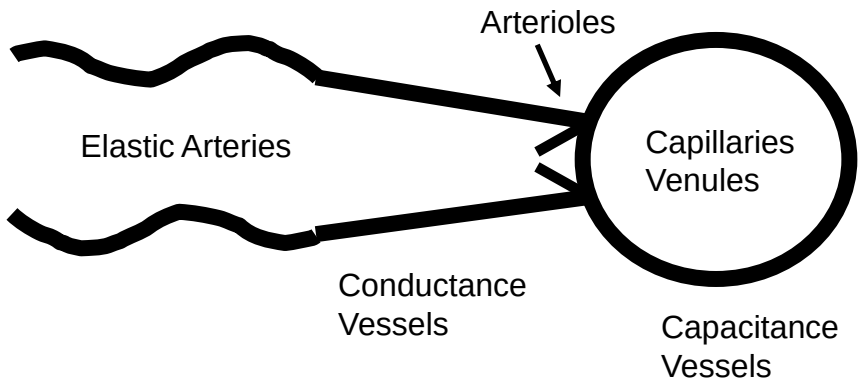
Cerebral Microbleeds Are Independently Associated with Arterial Stiffness in Stroke Patients

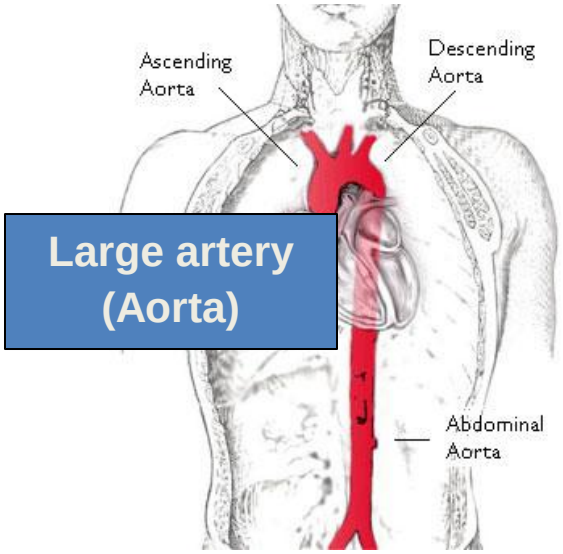
Woo-Keun Seo Jong-Moon Lee Moon Ho Park Kun Woo Park Dae Hie Lee

Department of Neurology, College of Medicine, Korea University Ansan Hospital, Ansan-city, Republic of Korea

Cerebrovasc Dis 2008;26:618–623

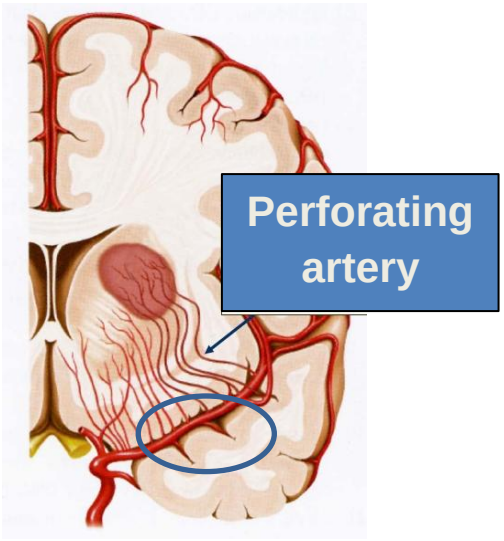
Relationship between PWV and Cerebral SVD





Large artery (Aorta)

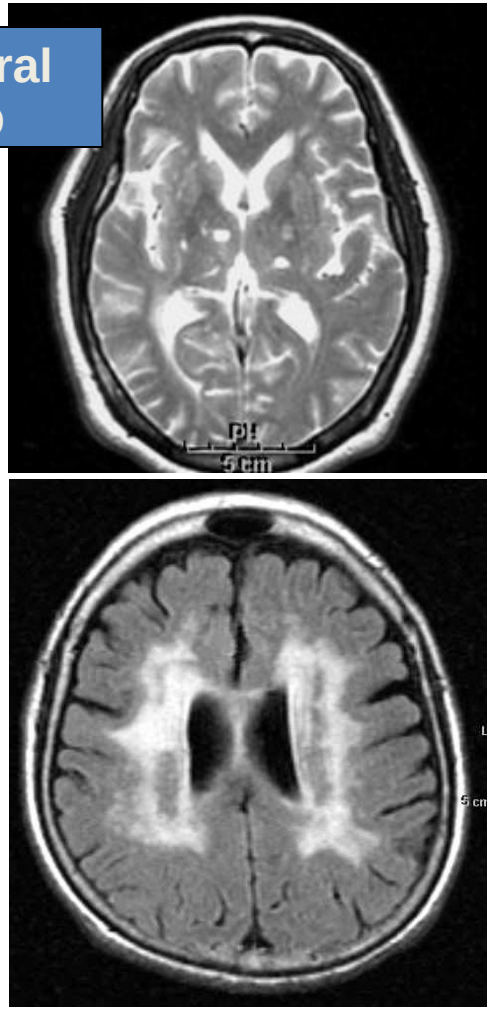
Pulse wave velocity
(Large artery stiffness)



Perforating artery

Pulsatile Index
(microvascular stiffness)

Cerebral SVD



Grading of CSVD

Arterial stiffness, PIs and severity of CSVD

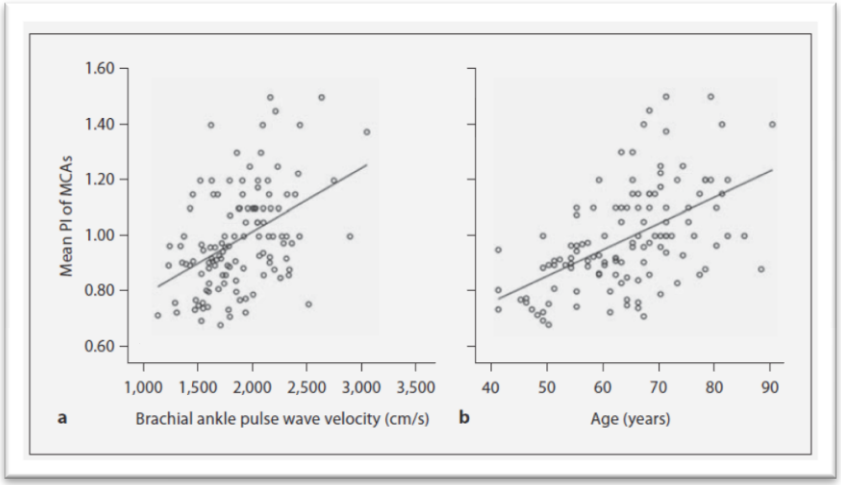


Table 2. Multiple regression analysis of the PI of MCA and associated variables

Independent variable	β coefficient	t value	p value
Age	0.008	4.659	<0.001
Sex	0.051	1.583	0.116
Pulse pressure	0.001	0.866	0.388
Heart rate	−0.001	−0.935	0.352
BaPWV	0.001	2.730	0.007

BaPWV = Brachial ankle pulse wave velocity; adjusted R^2 = 0.379.

Table 3. Multiple logistic regression analysis relating to the severity of CSVD

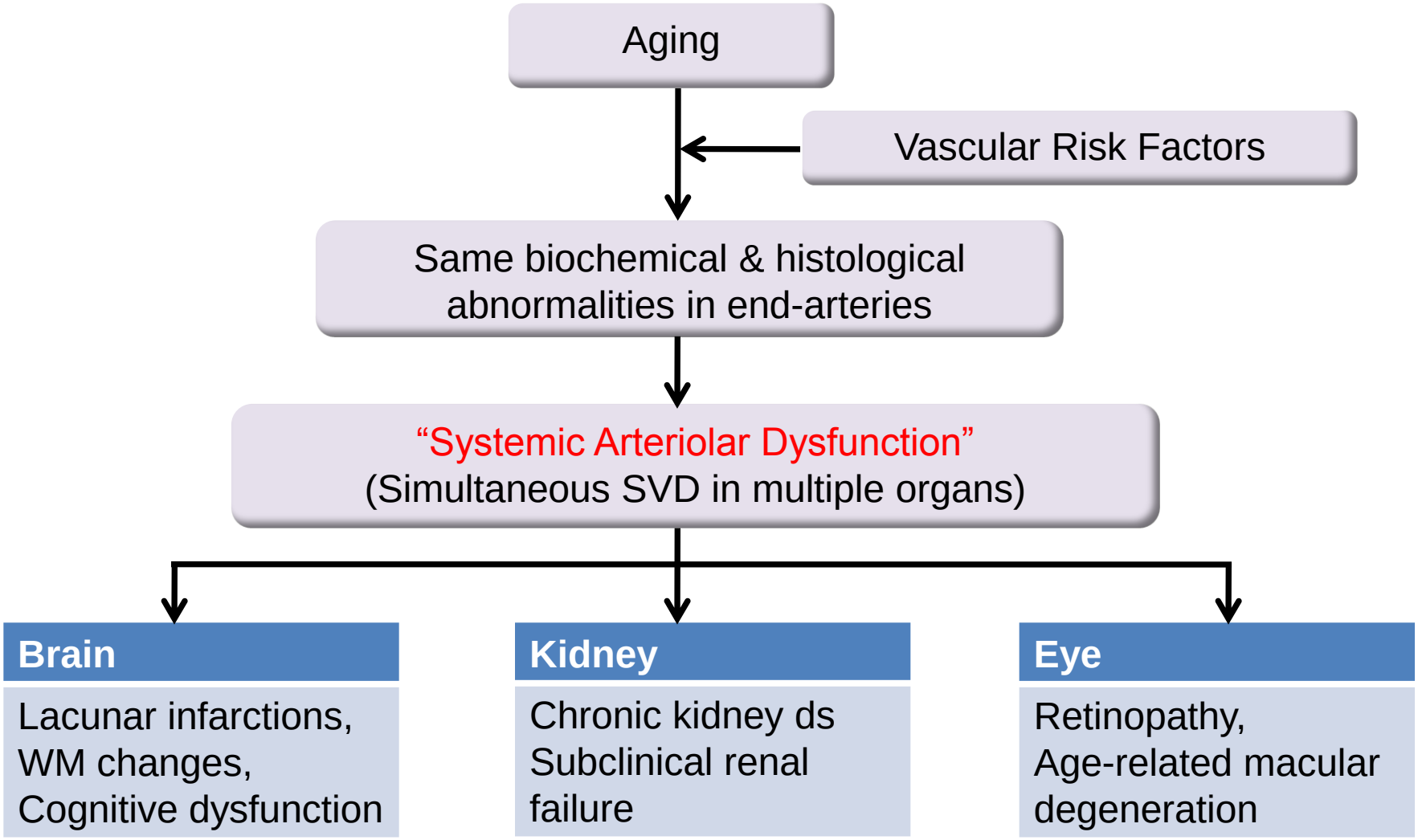
	Multiple lacunes		Moderate to severe white matter lesions	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.06 (1.01–1.12)	0.016	1.07 (1.01–1.14)	0.018
Male gender	0.61 (0.22–1.67)	0.340	1.79 (0.68–4.72)	0.233
Hypertension	2.54 (0.99–6.53)	0.052	2.38 (0.80–7.03)	0.115
Diabetes	0.51 (0.18–1.40)	0.196	0.58 (0.19–1.77)	0.589
BaPWV (100 cm/increment)	1.21 (1.02–1.44)	0.028	1.13 (0.95–1.35)	0.139
Initial systolic BP	1.00 (0.98–1.02)	0.478	1.00 (0.98–1.02)	0.956
Heart rate	1.00 (0.95–1.05)	0.930	1.01 (0.97–1.06)	0.424

Kime DH et al. Eur Neurol 2010;64:247–252

Cerebral SVD and clinical marker

- Increased SBP and pulse pressure
- Elevated 24-hour ambulatory blood pressure
- Small nocturnal fall in blood pressure
- Pathological changes in the retinal artery
- Microalbuminuria / subclinical renal disease
- Increased intima-media thickness of carotid artery

Hypothesis: Systemic Arteriolar Dysfunction



Thompson, C. S. et al. Stroke 2009;40:322-330

PWV and subclinical target organ damage

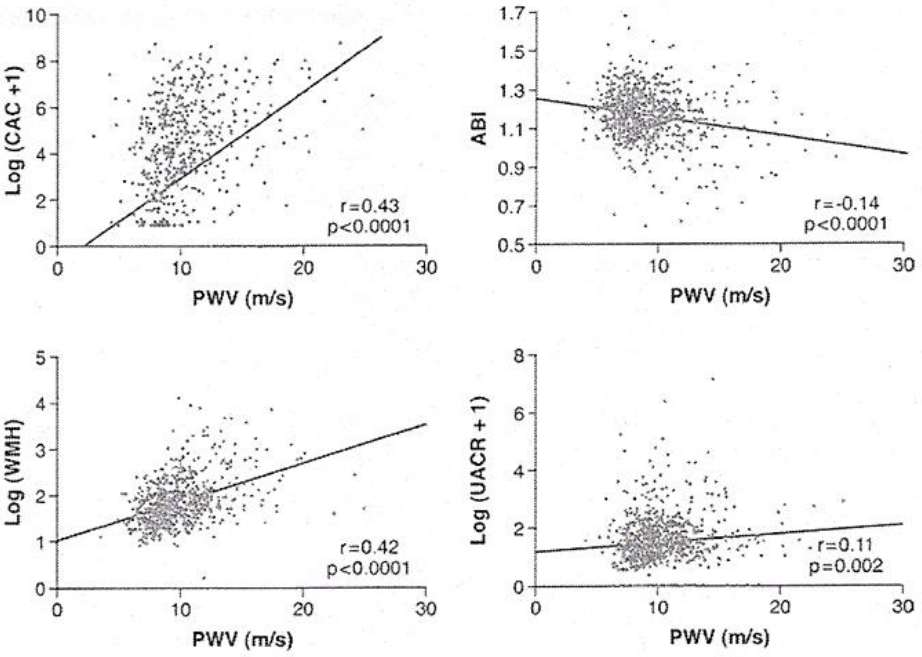


Figure 1. Correlations of aPWV With Coronary, Lower Extremity, Cerebral, and Renal Arteriosclerosis

Scatterplot depicting the unadjusted correlations of aortic pulse wave velocity (aPWV) with log (CAC + 1), ABI, log (WMH), and log (UACR + 1). ABI = ankle-brachial index; CAC = coronary artery calcification; UACR = urine albumin/creatinine ratio; WMH = brain white matter hyperintensity volume.

Coutinho et al. JACC 2011;4:754-61

Contents

Management of lacunar stroke

- Acute stage
  - Thrombolytic therapy
- Stroke prevention
  - Antiplatelet agent
  - Blood pressure control
  - Lipid lowering

Blood pressure control and WML change

- Perindopril Protection Against Recurrent Stroke Study (PROGRESS)
- MRI substudy (Cerebral WMHI in patients with stroke, N=192)
- MRI at baseline and follow-up (mean 3 years)
- Blood pressure reduction difference between active treatment and control (11.2 mmHg for SBP, 4.3 mmHg for DBP)

TABLE 4. Presence and Volume of Incident WMH by Treatment

	Total (n=192)	Placebo (n=103)	Active (n=89)	*P* Value, Model 1*	*P* Value, Model 2†
Incident WMH, n (%)	24 (13)	16 (16)	8 (9)	0.17	0.10
Mean volume of incident WMH, mm^3 (SE)	1.8 (0.5)	2.0 (0.7)	0.4 (0.8)	0.012	0.009
Volume of incident WMH by initial grade of WMH, mm^3 (SE)					
No WMH	0.05 (0.8)	0	0.09 (0.8)	0.76	0.81
Mild to moderate WMH	1.2 (1.2)	1.3 (1.0)	0.9 (1.0)	0.58	0.71
Severe WMH	6.5 (2.0)	7.6 (1.0)	0	<0.0001	<0.0001

Circulation 2005;112:1644

Conclusions

- The cerebral small arteries are exposed to high tensile pressure and susceptible to hemodynamic alterations
- Stiffening of the large arteries increases pulsatile pressure and flow stresses to the arterial walls, which extends down into the cerebral microvessels
- Higher aPWV was independently associated with greater burden of subclinical disease in cerebral small artery beds
- An active HT treatment can stop or delay the progression of cerebral SVD

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