

이광호교수님 퇴임기념

Vascular Calcification: From CT to Genomics



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I have nothing to disclose.

However,

I owe my inspiration for CT-based research to
Professor Kwang-Ho Lee.

Cortical sulcal effacement on brain CT associated with cerebral hyperperfusion after carotid artery stenting

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Byung Moon Kim^d, Gyeong-Moon Kim^{b,*}

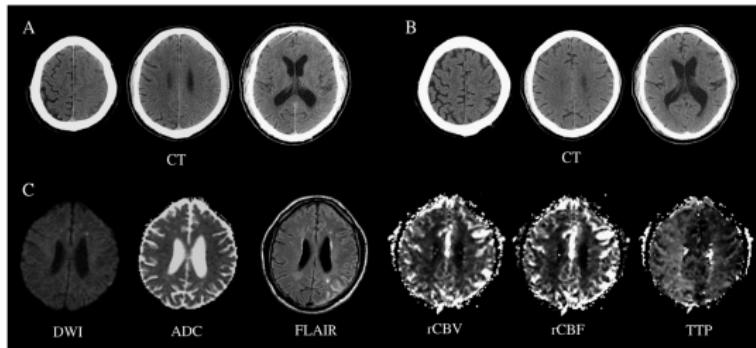
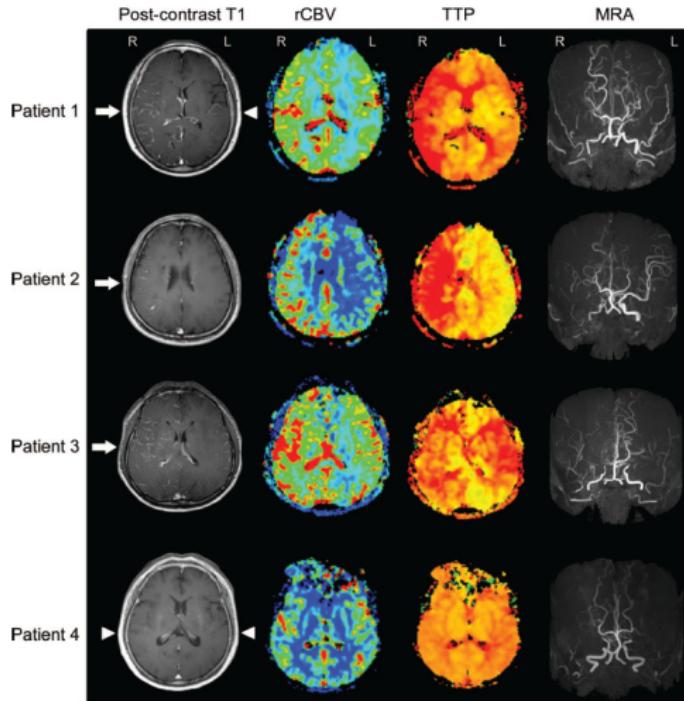


Fig. 1. (A) The non-enhanced brain CT performed 2 h after carotid artery stenting revealed diffuse sulcal effacement of the left hemisphere. (B) Ten days after stenting, there was an improvement in the degree of sulcal effacement. (C) Brain MRI revealed the presence of a few tiny ischemic lesions on DWI. Most of the regions showing sulcal effacement demonstrate no cytotoxic or vasogenic edema on the ADC map. A hyperintense area was observed in the cerebrospinal fluid spaces on FLAIR images. Perfusion-weighted MRI revealed a decreased TTP delay in the left hemisphere. DWI: diffusion-weighted imaging; ADC: apparent diffusion coefficient; FLAIR: fluid-attenuated inversion-recovery image; TTP: time to peak; rCBF: relative cerebral blood flow; rCBV: relative cerebral blood volume.

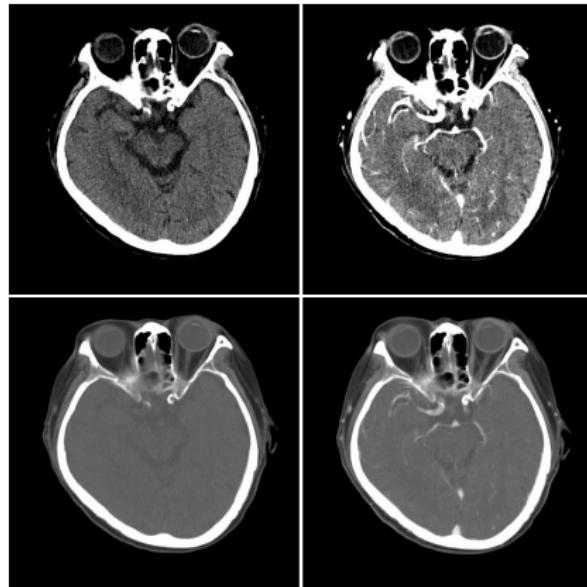
Figure

Perfusion pattern of the area showing leptomeningeal enhancement in patients with moyamoya disease

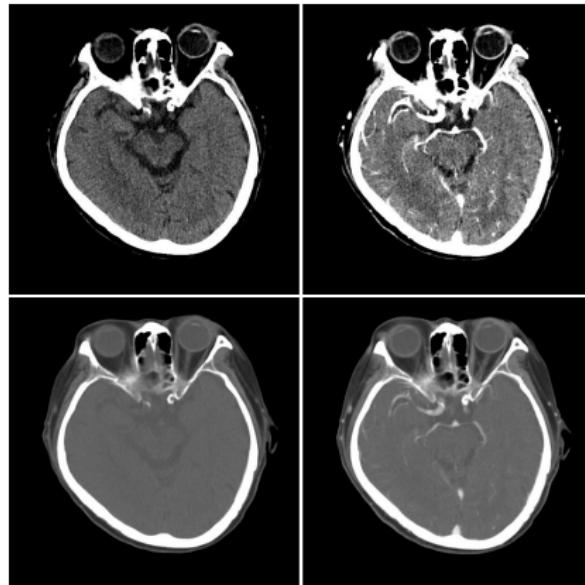


Chung PW and Park KY. Neurology 2009

76 YO female



76 YO female



- What could be the clinical significance of calcification?

- ① Introduction: vascular calcification
- ② Intracranial artery calcification on CT
- ③ Arterial stiffness and pulsatility
- ④ Vitamin D deficiency
- ⑤ SVD and genomic variations
- ⑥ Summary

Vascular Calcification

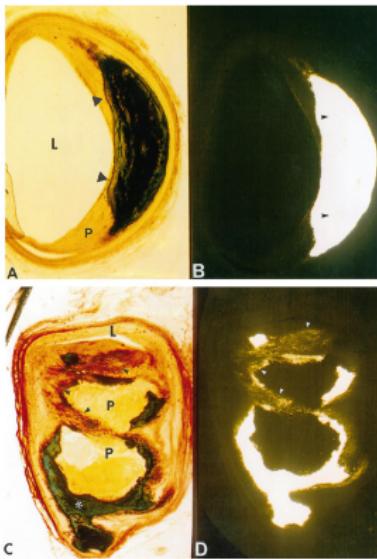
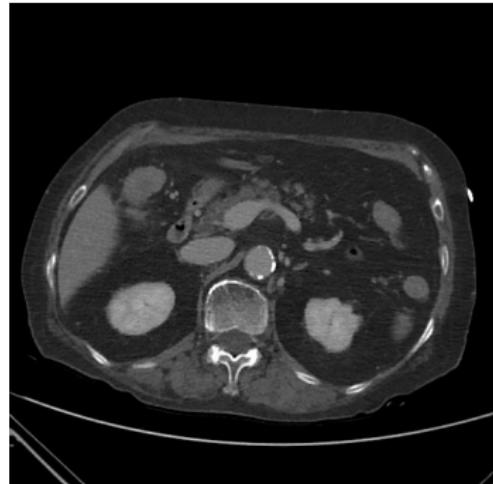


Figure 1. Photomicrographs of nondecalcified human coronary arteries. **A and B.**, Extensive calcium (arrowheads) is deposited relatively uniformly within a nonocclusive plaque (P), as shown by light microscopy (**A**, elastic van Gieson $\times 4$, reduced by 35%) and by microradiography (**B**). **C and D.**, In contrast, a large plaque with near total lumen (L) occlusion shows a large peripheral focus of dense calcium (asterisk) and a rim of microfocal mineralization (arrowheads) scattered distributed around the vessel circumference by light microscopy (**C**, elastic van Gieson $\times 2$, reduced by 35%) and by microradiography (**D**).

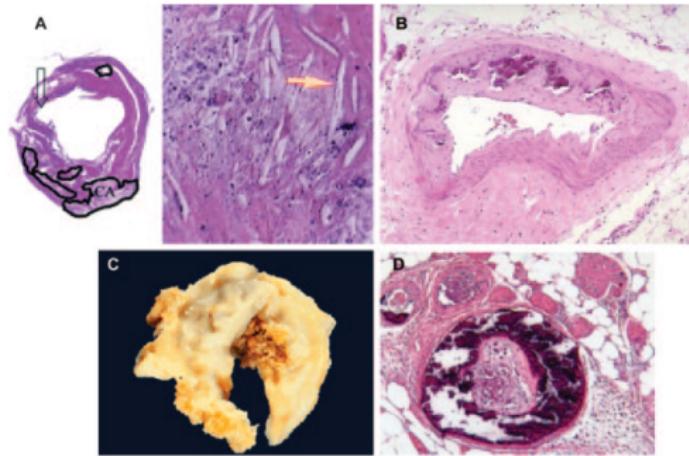
Vascular calcification was considered to be

- a passive phenomenon of aging
- an inert end-point of atherosclerosis



Vascular calcification is an actively regulated process that resembles orthotopic bone formation

Type of calcification

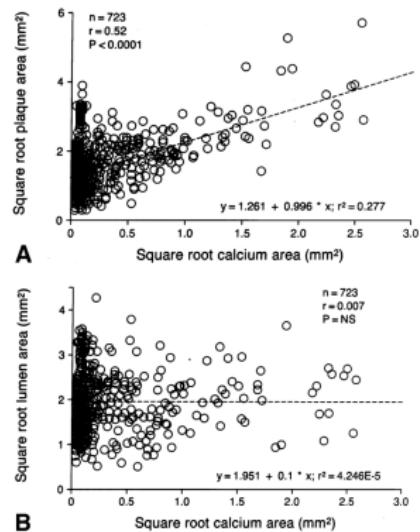


- A Atherosclerotic calcification
- B Medial calcification
- C Valvular calcification
- D Calciphylaxis

Johnson RC et al. Circ Res. 2006

Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden

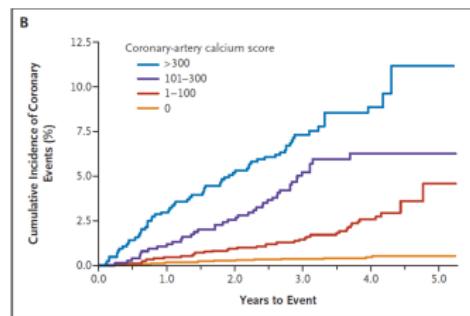
- Square root of **coronary calcium area** detected by histopathologic and microradiographic analysis vs. square root of **plaque area**



Sangiorgi G et al. J Am Coll Cardiol. 1998.

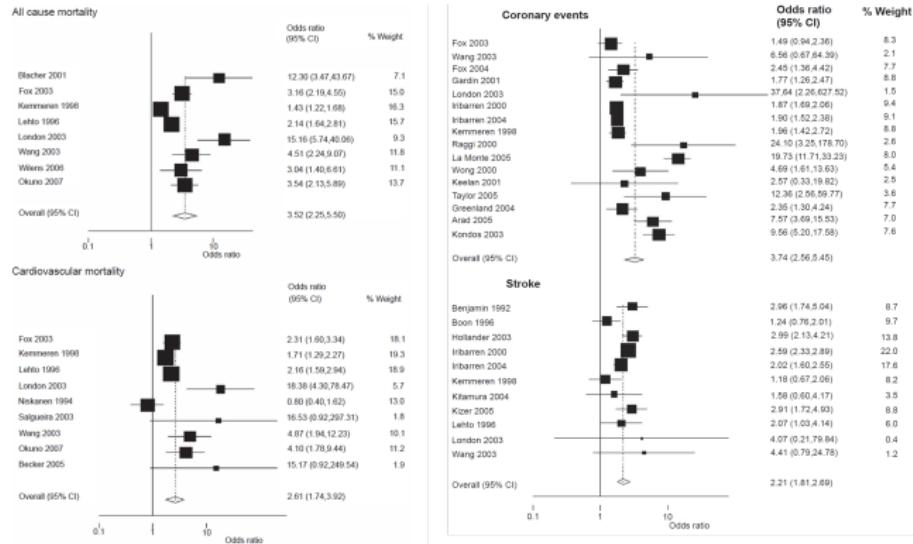
Coronary calcium as a predictor of coronary events

- In comparison with participants with **no coronary calcium**, adjusted risk of a coronary events was increased by a factor of **9.67** among participants with **calcium score above 300** ($p < 0.001$)



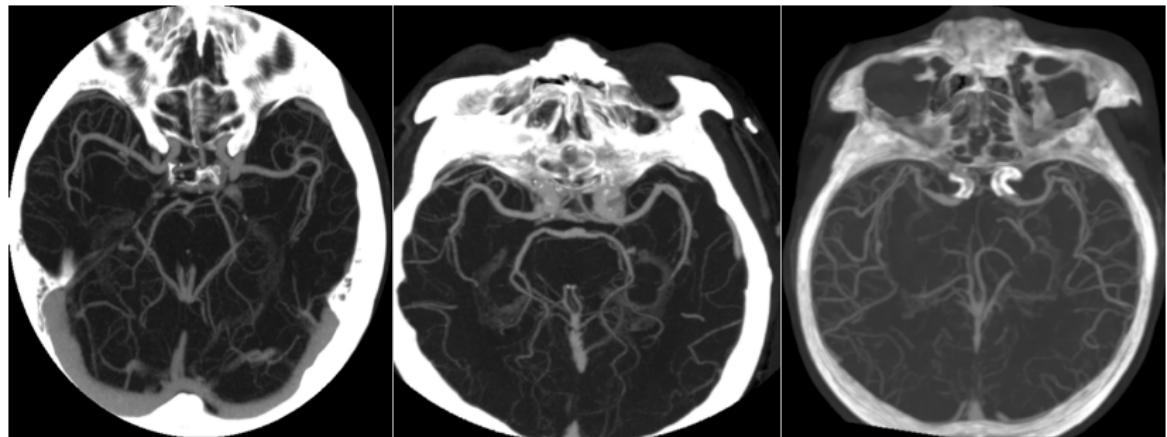
Detrano R et al. N Eng J Med. 2008.

Vascular calcification is a marker of increased cardiovascular risk: A meta-analysis

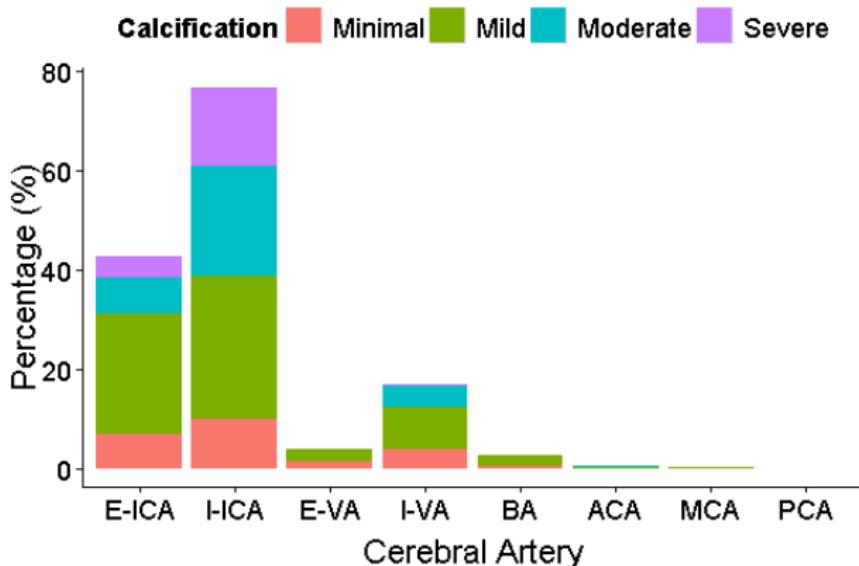


Rennenberg RJMW et al. Vasc Health Risk Manag. 2009.

Intracranial Artery Calcification



Intracranial ICA can be a representative for cerebral artery calcification



Chung PW et al. Cerebrovasc Dis. 2010

Intracranial ICA calcification is associated with lacunes

	Lacunes	
	OR	p
Crude OR	5.29 (2.97 - 9.42)	<0.001
Adjusted OR, model 1	3.15 (1.68 - 5.91)	<0.001
Adjusted OR, model 2	3.09 (1.64 - 5.83)	<0.001
Adjusted OR, model 3	2.67 (1.35 - 5.26)	0.005

Table: Calcification and lacune

Model 1 was adjusted for age, model 2 for age and sex, and model 3 for age, sex, hypertension and diabetes mellitus.

Intracranial ICA calcification is associated with WMH

	Subcortical WMH	
	OR	p
Crude OR	5.74 (2.87 - 11.5)	<0.001
Adjusted OR, model 1	3.06 (1.46 - 6.42)	0.003
Adjusted OR, model 2	3.25 (1.53 - 6.89)	0.002
Adjusted OR, model 3	2.46 (1.07 - 5.61)	0.033

Table: Calcification and subcortical white matter hyperintensity

Model 1 was adjusted for age, model 2 for age and sex, and model 3 for age, sex, hypertension, diabetes mellitus, current smoking, hyperlipidemia, and stroke history.

Intracranial ICA calcification is associated with deep CMB

	Mild calcification		Severe calcification	
	OR	p	OR	p
CMB of any location				
Crude OR	2.14 (1.65–2.77)	<0.0001	4.22 (3.19–5.59)	<0.0001
Adjusted OR	1.76 (1.31–2.36)	0.0002	2.86 (2.01–4.08)	<0.0001
Deep CMB				
Crude OR	2.07 (1.55–2.76)	<0.0001	5.01 (3.71–6.78)	<0.0001
Adjusted OR	1.76 (1.30–2.44)	0.0007	3.51 (2.39–5.14)	<0.0001
Strictly lobar CMB				
Crude OR	1.70 (1.02–2.82)	0.04	1.01 (0.55–1.84)	0.98
Adjusted OR	1.57 (0.90–2.76)	0.11	0.90 (0.47–1.74)	0.75

Values in parentheses are 95% CI. Adjusted OR was calculated using multivariable analysis whose entered variables were age, hypertension, previous stroke history, hs-CRP, total cholesterol, homocysteine, and ICA calcification.

Arterial stiffness and pulsatility

Arterial Stiffness

- Increased arterial stiffness might be explained by deposition of circulating calcific microparticles or the *in situ* formation of vascular microcalcifications

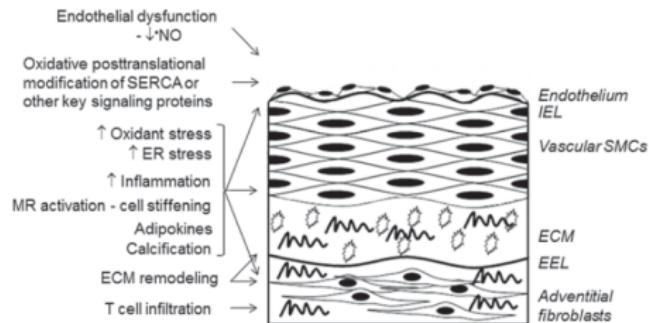


Figure. Cellular and molecular mechanisms of arterial stiffening.

Jeopard JA. Hypertension. 2013; Safar ME et al. Am J Physiol Heart Circ Physiol. 2007.

Arterial Stiffness

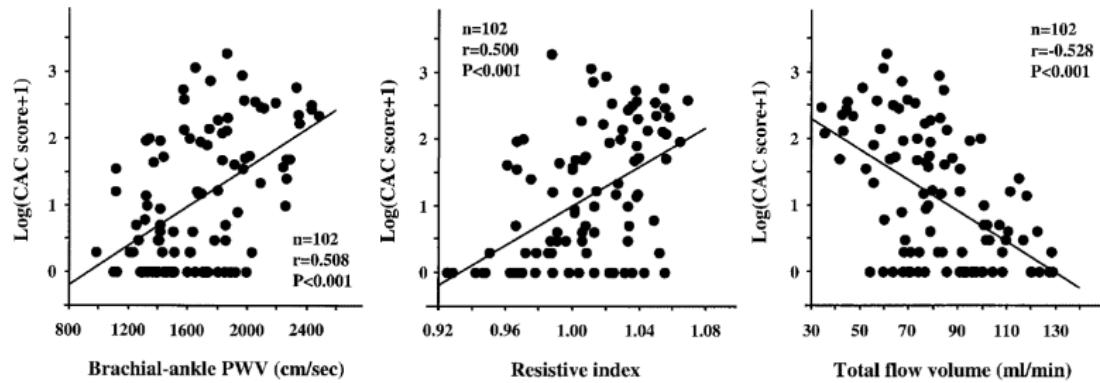


Figure 3—Simple linear regression analyses of the relationship between brachial-ankle PWV (A), resistive index (B), and total flow volume (C) at the popliteal artery and log-transformed Agatston CAC score for all 102 asymptomatic diabetic patients.

Tsuchiya M et al. Diabetes Care. 2004.

Potential Mechanism: Arterial Stiffening

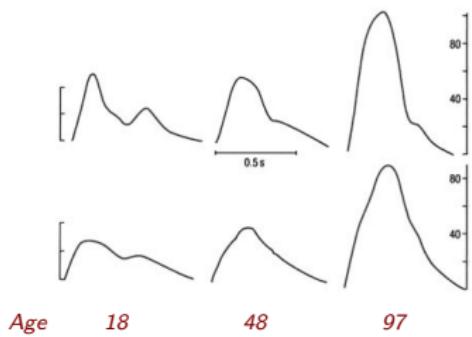
Relationship Between Aortic Stiffening and Microvascular Disease in Brain and Kidney Cause and Logic of Therapy

Michael F. O'Rourke, Michel E. Safar

Abstract—A close relationship has been established between microvascular damage in brain and kidney and indices of age and hypertension (pulse pressure, aortic pulse wave velocity, and augmentation index). The mechanism of such association has not been established, nor has rationale for prevention and treatment of microvascular damage. A logical pathophysiological explanation can be offered on the basis of differential input impedance in the brain and kidney compared with other systemic vascular beds. Torrential flow and low resistance to flow in these organs exposes small arterial vessels to the high-pressure fluctuations that exist in the carotid, vertebral, and renal arteries. Such fluctuations, measurable as central pulse pressure, increase 3- to 4-fold with age. Exposure of small vessels to highly pulsatile pressure and flow explains microvascular damage and resulting renal insufficiency and intellectual deterioration, according to the mechanism established by Byrom >50 years ago. The logical approach to prevention and treatment requires reduction of central pulse pressure. Because the aorta and large arteries are not directly affected by drugs, this entails reduction of wave reflection by dilation of conduit arteries elsewhere in the body. This can be accomplished by regular exercise and by drugs such as nitrates, calcium channel blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers. The explanation given here accounts for greater and earlier vascular damage in diabetes mellitus (relative microvascular fragility) and is similar to that given for vascular changes of pulmonary hypertension caused by ventricular septal defects and other congenital vascular shunts. (*Hypertension*. 2005;46:200-204.)

Key Words: arterial pressure ■ microcirculation ■ pulse ■ cerebrovascular disorders ■ renal disease

Potential Mechanism: Arterial Stiffening



these organs while mean flow is maintained.³⁶ Brain and kidney arteries of all sizes are thus subjected to higher pulsatile circumferential stress and higher longitudinal shear stress. Their ability to withstand increased stresses depends on their resilience, and this is markedly decreased in a number of diseases, particularly diabetes mellitus.^{11,12,34} Aging changes of large arteries thus promote a “set-up” for small arterial disease and the types of changes elegantly elucidated by Byrom and others 50 years ago.^{36–38}

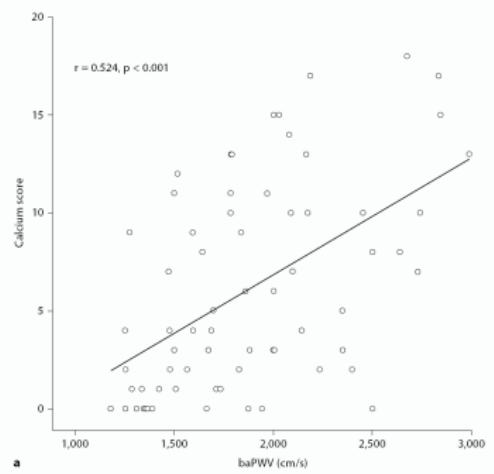
Effects of Arterial Stiffening on the Kidney and Brain Microvasculature

Byrom's work was initially conducted on rats but was applied to the small-vessel disease seen in human hypertension.^{37,38} He showed that damage to small arteries could be induced by increased pulsatile stress and could lead to tearing of their endothelial and smooth muscle cells with disruption of the vessel. He thus explained development of small arterial dilations and aneurysms, and the features of lipohyalinoses and of fibrinoid necrosis as seen in the brains and kidneys of

O'Rourke MF et al. Hypertension. 2005; Byrom FB. Lancet. 1954

Cerebral Arterial Calcification is Associated with Systemic Arterial Stiffness

- Arterial stiffness, as measured by brachial-ankle pulse wave velocity (baPWV)
- Age and cerebral arterial calcification were independent determinants of baPWV.



Park KY et al. Eur Neurol. 2009



Brachial-ankle pulse wave velocity is associated with both acute and chronic cerebral small vessel disease



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Cerebral microbleed

ABSTRACT

Objective: The aim of this study was to determine the association of brachial-ankle pulse wave velocity (baPWV) with both acute and chronic cerebral small vessel disease (SVD).

Methods: We identified 1282 consecutive patients with acute ischemic stroke or transient ischemic attack. Neuroimaging correlates of chronic lacunes, white matter hyperintensity (WMH), and cerebral microbleed (CMB) were assessed using MR images. Combined SVD score was defined as the number of presence of SVD markers including chronic lacunes, WMH, deep CMB, and acute lacunar infarction. The association between baPWV and SVD was tested using linear and logistic regression analyses.

Results: Mean age of patients was 68 (± 12) years. Chronic lacunes were found in 675 patients (53%), WMH in 970 patients (77%), and deep CMB in 349 patients (30%). Among the 1145 patients with ischemic stroke, 292 patients (26%) were classified as having acute SVD. On multivariate analysis, a 1-SD increase in baPWV was associated with chronic lacunes [odds ratio, 1.24; 95% CI, 1.07–1.44; $p < 0.01$], WMH (1.38; 1.13–1.71; $p < 0.01$), deep CMB (1.29; 1.11–1.51; $p < 0.01$), acute SVD (1.19; 1.01–1.40; $p = 0.04$), combined SVD score > 1 (1.27; 1.06–1.53; $p = 0.01$), and combined SVD score > 2 (1.40; 1.19–1.65; $p < 0.01$).

Conclusions: baPWV is associated with both acute and chronic SVD. Our findings suggest that arterial stiffness is linked to the pathogenesis of SVD. Also, baPWV could be used as a biomarker of SVD. In future trials, it should be tested whether arterial stiffness can be a therapeutic target for SVD.

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1802 patients with acute ischemic stroke or TIA

520 were excluded because
both diffusion-weighted imaging and pulse-wave
measurement were not available

1282 patients were eligible for study.

1145 patients with acute ischemic stroke

Chronic lacune found in 619
WMH found in 881
Deep CMB found in 331
Acute small vessel occlusion in 292

137 patients with TIA

Chronic lacune found in 56
WMH found in 89
Deep CMB found in 18

PWV, 5m/sec	Lacunes	
	OR	p
Crude OR, model 1	1.58 (1.40 – 1.79)	<0.01
Adjusted OR, model 2	1.27 (1.10 – 1.47)	<0.01
Adjusted OR, model 3	1.24 (1.07 – 1.44)	<0.01
PWV, 5m/sec	WMH	
	OR	p
Crude OR, model 1	2.35 (1.98 – 2.80)	<0.01
Adjusted OR, model 2	1.42 (1.16 – 1.75)	<0.01
Adjusted OR, model 3	1.38 (1.13 – 1.71)	<0.01
PWV, 5m/sec	Deep CMB	
	OR	p
Crude OR, model 1	1.45 (1.29 – 1.65)	<0.01
Adjusted OR, model 2	1.30 (1.12 – 1.52)	<0.01
Adjusted OR, model 3	1.29 (1.11 – 1.51)	<0.01

Table: baPWV and chronic SVD

Model 1 is the bivariate analysis. Model 2 is adjusted for age, sex, hypertension, diabetes mellitus, current smoking, previous stroke history, systolic blood pressure, diastolic blood pressure, HDL-cholesterol, and glycated hemoglobin. Model 3 is adjusted for atrial fibrillation, total cholesterol, LDL-cholesterol, and the variables entered in model 2.

PWV, 5m/sec	SVO	
	OR	p
Crude OR, model 1	1.16 (1.02 – 1.32)	0.02
Adjusted OR, model 2	1.27 (1.09 – 1.48)	<0.01
Adjusted OR, model 3	1.19 (1.01 – 1.40)	0.04
PWV, 5m/sec	LAA	
	OR	p
Crude OR, model 1	1.00 (0.89 – 1.13)	0.94
Adjusted OR, model 2	0.96 (0.83 – 1.11)	0.61
Adjusted OR, model 3	0.88 (0.75 – 1.03)	0.11
PWV, 5m/sec	CE	
	OR	p
Crude OR, model 1	1.00 (0.87 – 1.15)	0.99
Adjusted OR, model 2	0.74 (0.61 – 0.88)	<0.01
Adjusted OR, model 3	0.74 (0.61 – 0.88)	<0.01

Table: baPWV and acute SVD

Model 1 is the bivariate analysis. Model 2 is adjusted for age, sex, hypertension, diabetes mellitus, ischemic heart disease, current smoking, systolic blood pressure, diastolic blood pressure, HDL-cholesterol, and glycated hemoglobin. Model 3 is adjusted for atrial fibrillation, previous stroke history, total cholesterol, LDL-cholesterol, and the variables entered in model 2.

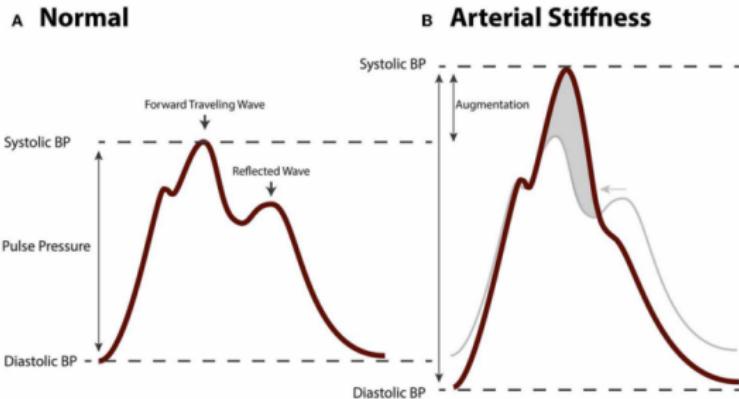
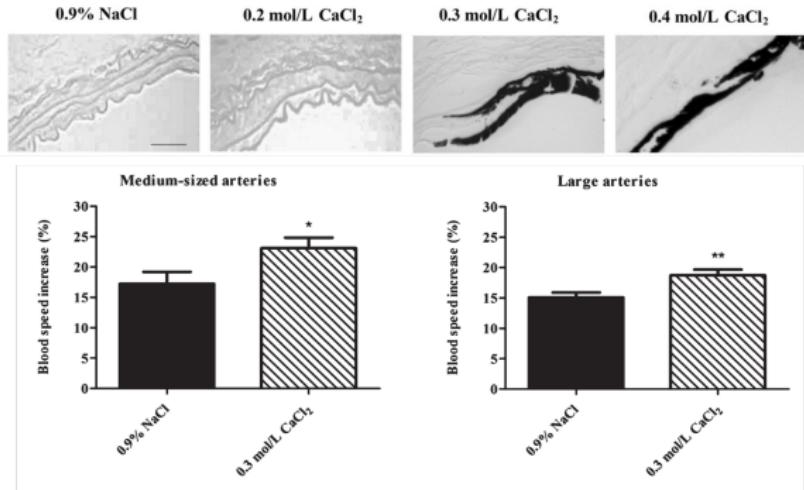


FIGURE 4 | Hemodynamic changes in arterial stiffening. (A) Aortic blood pressure waveform of a healthy, normotensive person. The forwards traveling wave precedes the (backwards traveling) reflected wave. **(B)** Aortic pressure

waveform of a person with arterial stiffness. Due to increased pulse wave velocity, the forward traveling wave and reflected wave are summated leading to augmented pulse pressure.

Increased pulsatility is associated with ICA calcification: Animal Study



Sadekova N et al. J Am Heart Assoc. 2013

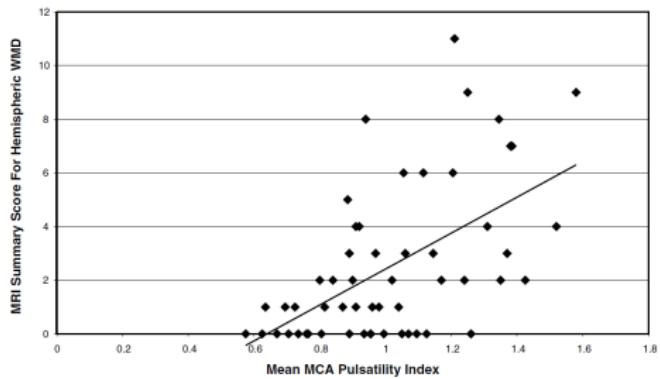
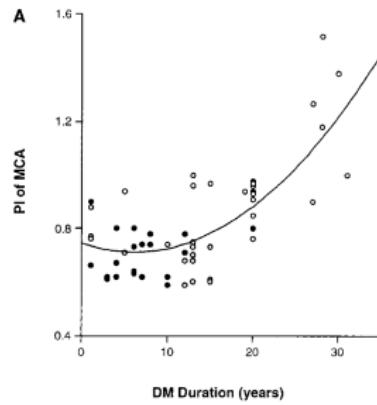
Increased pulsatility index is associated with ICA calcification

Table 2. Clinical characteristics in relation to PI

	PI quartiles				p
	1st (n = 39) 0.515–0.811	2nd (n = 39) 0.812–0.914	3rd (n = 39) 0.921–1.058	4th (n = 39) 1.06–1.529	
Demographics					
Age, years	52.1 ± 11.8	60.4 ± 11.5	65.6 ± 9.4	70.6 ± 12.1	<0.001
Male sex	25 (64.1)	23 (59.0)	24 (61.5)	28 (71.8)	0.457
Hypertension	20 (51.3)	21 (53.8)	18 (46.2)	22 (56.4)	0.83
Diabetes	12 (30.8)	13 (33.3)	20 (51.3)	20 (51.3)	0.025
Hypercholesterolemia	10 (25.6)	11 (28.2)	7 (17.9)	8 (20.5)	0.397
Coronary artery disease	2 (5.2)	4 (10.3)	4 (10.3)	3 (7.7)	0.698
Atrial fibrillation	4 (10.3)	1 (2.6)	2 (5.2)	3 (7.7)	0.771
Prior stroke	3 (7.7)	5 (12.8)	2 (5.2)	7 (17.9)	0.303
Exposure to smoking	16 (41.0)	14 (35.9)	6 (15.4)	10 (25.6)	0.042
Admission profiles					
Systolic BP, mm Hg	136.9 ± 23.0	138.7 ± 25.2	146.9 ± 21.7	139.8 ± 21.8	0.11
Total cholesterol, mg/dl	189.6 ± 44.1	195.9 ± 52.4	182.5 ± 38.8	182.5 ± 41.6	0.729
Fasting glucose, mg/dl	134.4 ± 66.2	125.9 ± 59.6	133.6 ± 67.5	135.9 ± 68.5	0.823
HbA1c, %	6.1 ± 1.3	6.2 ± 1.5	6.6 ± 1.8	6.4 ± 1.6	0.528
ICAC score	1.6 ± 1.8	2.1 ± 1.9	2.8 ± 2.2	3.9 ± 1.7	<0.001

Park KY et al. Eur Neurol. 2013

Pulsatility Index and small vessel disease



Lee KY et al. Stroke. 2000; Kidwell CS et al. J Neuroimaging. 2001

Risk factors of vascular calcification

- Associated conditions
 - Age
 - Hypertension
 - Hyperlipidemia
 - Chronic kidney disease
 - Diabetes
 - Osteoporosis
 - Hyperparathyroidism

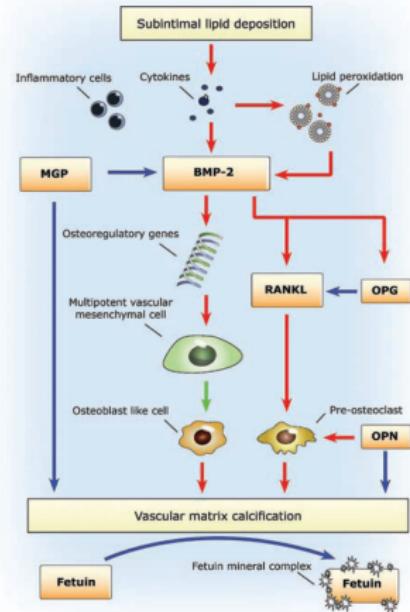


Fig. 1 Blue arrows indicate an inhibiting effect and red arrows indicate a stimulating effect.

Rennenberg RJMW et al. J. Cell. Mol. Med. 2010

Vitamin D

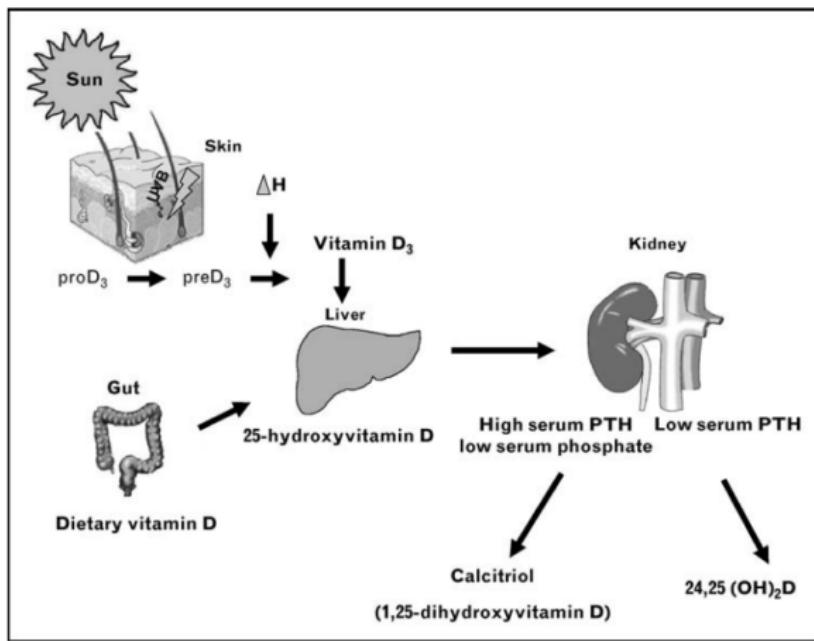
- Calcium homeostasis and bone metabolism

Vitamin D

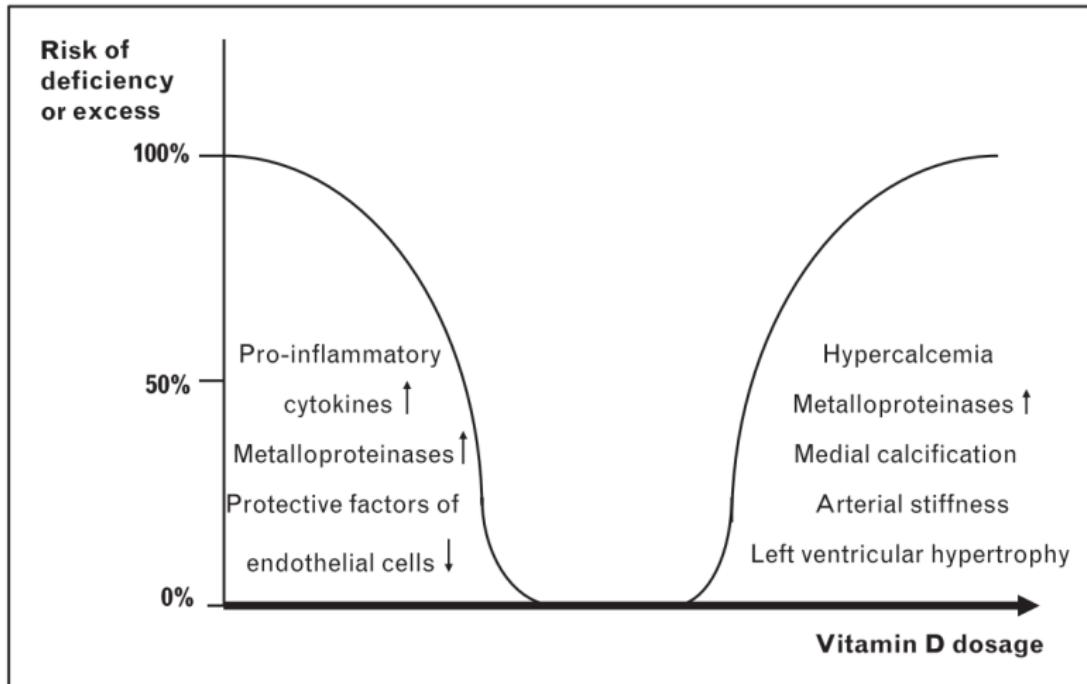
- Calcium homeostasis and bone metabolism
- Atherosclerosis
- Blood pressure
- Inflammation
- Metabolic syndrome
- Vascular calcification
- Arterial stiffness

Figure 1 Vitamin D physiology

PTH, parathyroid hormone. Adapted with permission [1].



Zittermann A. et al. *Curr Opin Lipidol* 2007



Zittermann A. et al. Curr Opin Lipidol 2007

25-Hydroxyvitamin D Status Is Associated With Chronic Cerebral Small Vessel Disease

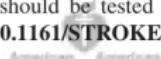
Pil-Wook Chung, MD; Kwang-Yeol Park, MD; Jeong-Min Kim, MD; Dong-Woo Shin, MD; Moo-Seok Park, MD; Yun Jae Chung, MD; Sam-Yeol Ha, MD; Suk-Won Ahn, MD; Hae-Won Shin, MD; Yong Bum Kim, MD; Heui-Soo Moon, MD

Background and Purpose—The aim of this study was to determine the association between 25-hydroxyvitamin D (25(OH)D) and neuroimaging correlates of cerebral small vessel disease.

Methods—We identified 759 consecutive patients with acute ischemic stroke or transient ischemic attack. Lacunes, white matter hyperintensity, and cerebral microbleed (CMB) were assessed using MR images. Deep CMB was defined as the presence of CMB in basal ganglia, thalamus, or brain stem. The association between 25(OH)D and small vessel disease was tested using linear and logistic regression analyses.

Results—Mean age was 68 (± 13) years. Mean level of 25(OH)D was 34.1 ± 17.8 nmol/L. On bivariate analysis, a 25-nmol/L decrease in 25(OH)D was associated with lacunes (regression coefficient, 0.23; 95% confidence interval [CI], 0.02–0.45), severe white matter hyperintensity (odds ratio, 2.05; 95% CI, 1.41–3.08), and deep CMB (odds ratio, 1.28; 95% CI, 1.01–1.63). Also, 25(OH)D deficiency (≤ 25 nmol/L) was associated with lacunes (regression coefficient, 0.5; 95% CI, 0.04–0.95), severe white matter hyperintensity (odds ratio, 2.74; 95% CI, 1.31–6.45), and deep CMB (odds ratio, 1.68; 95% CI, 1.03–2.78). The association remained significant even after multivariable adjustment and in the subgroup of previously healthy patients.

Conclusions—25(OH)D is inversely associated with lacunes, white matter hyperintensity, and deep CMB. Our findings suggest that 25(OH)D is linked to small vessel disease, and in future trials it should be tested whether 25(OH)D supplementation can prevent small vessel disease. (*Stroke*. 2015;46:00-00. DOI: 10.1161/STROKEAHA.114.007706)



Chung PW et al. *Stroke* 2015

- The mean age of 759 patients was 68 (± 13) years.
- Mean level of 25(OH)D was 34.1 (± 17.8) nmol/L.
- The levels of 25(OH)D were classified as
 - sufficient in 122 patients (16%),
 - insufficient in 358 patients (47%), and
 - deficient in 279 patients (37%).

Chung PW et al. Stroke 2015

Table 2. Association Between 25(OH)D and Cerebral Small Vessel Disease

	Lacunes		WMH		Deep Microbleed	
	RC (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
A 25-nmol/L decrease in 25(OH)D						
Model 1	0.23 (0.02–0.45)	0.03	2.05 (1.41–3.08)	<0.01	1.28 (1.01–1.63)	0.04
Model 2	0.26 (0.05–0.47)	0.01	1.82 (1.24–2.77)	<0.01	1.29 (1.01–1.65)	0.04
Model 3	0.26 (0.05–0.48)	0.02	1.79 (1.21–2.73)	<0.01	1.34 (1.05–1.72)	0.02
25(OH)D, 3 groups						
Model 1						
Sufficient	Reference	...	Reference	...	Reference	...
Insufficient	0.47 (0.03–0.91)	0.04	1.59 (0.75–3.77)	0.26	1.34 (0.84–2.19)	0.23
Deficient	0.50 (0.04–0.95)	0.03	2.74 (1.31–6.45)	0.01	1.68 (1.03–2.78)	0.04
Model 2						
Sufficient	Reference	...	Reference	...	Reference	...
Insufficient	0.47 (0.05–0.89)	0.03	1.78 (0.82–4.35)	0.17	1.42 (0.87–2.35)	0.16
Deficient	0.54 (0.10–0.98)	0.02	2.60 (1.20–6.29)	0.02	1.73 (1.05–2.91)	0.04
Model 3						
Sufficient	Reference	...	Reference	...	Reference	...
Insufficient	0.46 (0.03–0.89)	0.04	1.71 (0.77–4.19)	0.21	1.50 (0.91–2.52)	0.11
Deficient	0.54 (0.09–0.99)	0.02	2.47 (1.13–6.05)	0.03	1.84 (1.10–3.14)	0.02

Model 1 is the bivariate analysis. Model 2 is adjusted for age, sex, hypertension, diabetes mellitus, white blood cell, total cholesterol, triglyceride, and glycohemoglobin. Model 3 is adjusted for calcium, phosphorus, and the variables entered in model 2. 25(OH)D indicates 25-hydroxyvitamin D; CI, confidence interval; OR, odds ratio; RC, regression coefficient; and WMH, white matter hyperintensity.

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Serum Vitamin D Status as a Predictor of Prognosis in Patients with Acute Ischemic Stroke

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Bum-Chun Suh^b Yu Sam Won^c Jeong-Min Kim^a Young Chul Youn^a
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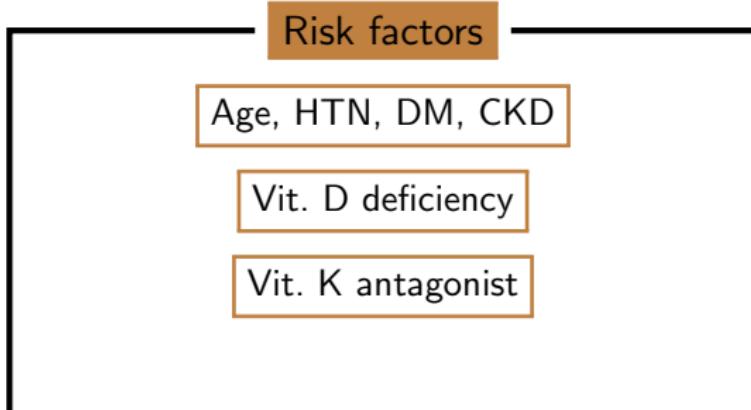
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Park KY et al. Cerebrovasc Dis 2015

Table 4. OR (95% CI) of 3-month good outcome (mRS = 0, 1, 2) for 25(OH)D according to month-specific quartiles of 25(OH)D and absolute 25(OH)D level status

Serum 25(OH)D	Model 1		Model 2		Model 3	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Lowest quartile	1 (Reference)		1 (Reference)		1 (Reference)	
2nd quartile	1.43 (0.96–2.12)	0.079	1.52 (0.96–2.40)	0.075	1.40 (0.85–2.31)	0.188
3rd quartile	1.48 (0.99–2.20)	0.054	1.62 (1.03–2.55)	0.038	1.66 (1.01–2.73)	0.047
Highest quartile	1.68 (1.13–2.51)	0.011	1.70 (1.07–2.69)	0.025	1.90 (1.14–3.16)	0.014
<25 nmol/l	1 (Reference)		1 (Reference)		1 (Reference)	
25–50 nmol/l	1.52 (1.04–2.21)	0.03	1.47 (0.96–2.26)	0.079	1.32 (0.82–2.11)	0.250
50–75 nmol/l	1.5 (0.95–2.38)	0.083	1.56 (0.92–2.63)	0.097	1.80 (1.00–3.23)	0.050
≥75 nmol/l	2.02 (1.22–3.33)	0.006	1.98 (1.11–3.51)	0.020	2.40 (1.25–4.62)	0.009

Model 1 includes age, sex and 25(OH)D. Model 2 includes model 1 and adds hypertension, diabetes, atrial fibrillation, stroke history, leukocyte count, hemoglobin, fasting glucose, high-sensitivity C-reactive protein and fasting triglyceride level. Model 3 includes model 2 and admission NIHSS score and stroke subtypes.



Intracranial Artery Calcification

Arterial stiffness

Increased pulsatility

Cerebral small vessel disease

Vascular calcification

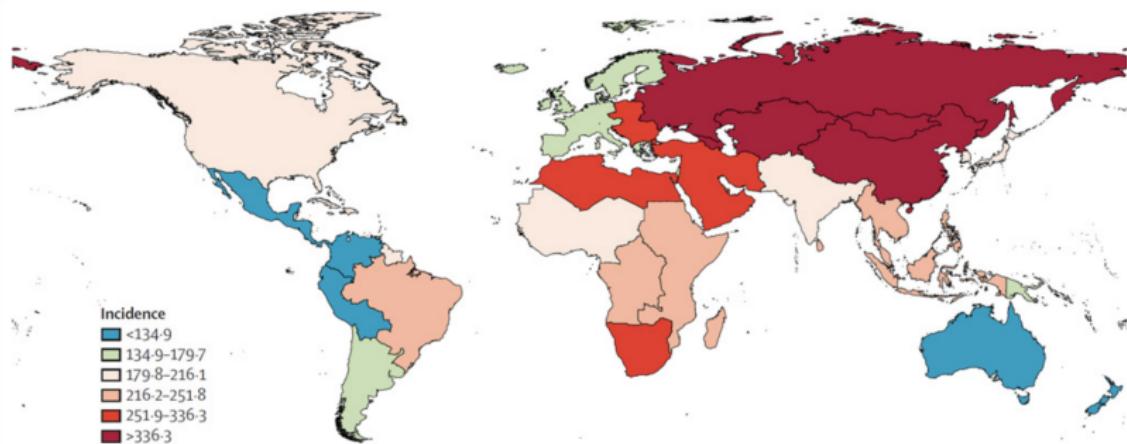
Arterial stiffness

Increased pulse pressure

CV morbidity and mortality

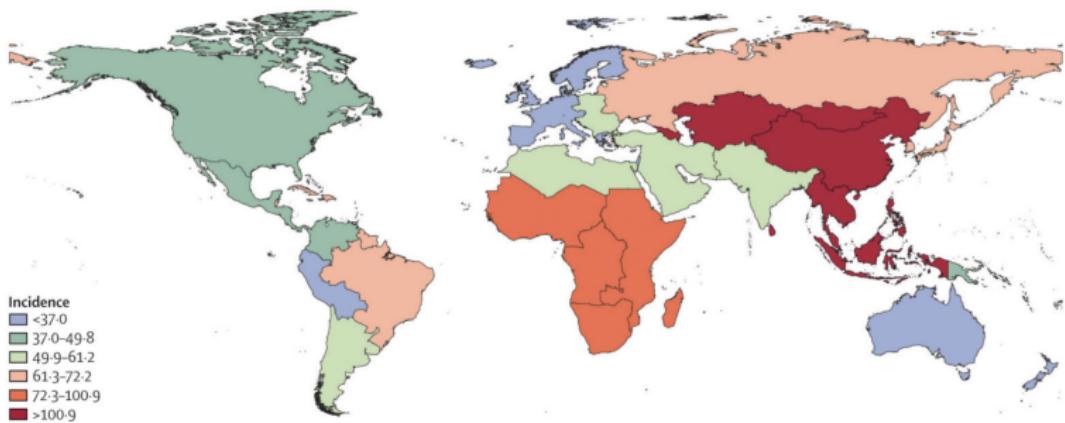
Age-standardised stroke incidence

per 100 000 person-years for 2010



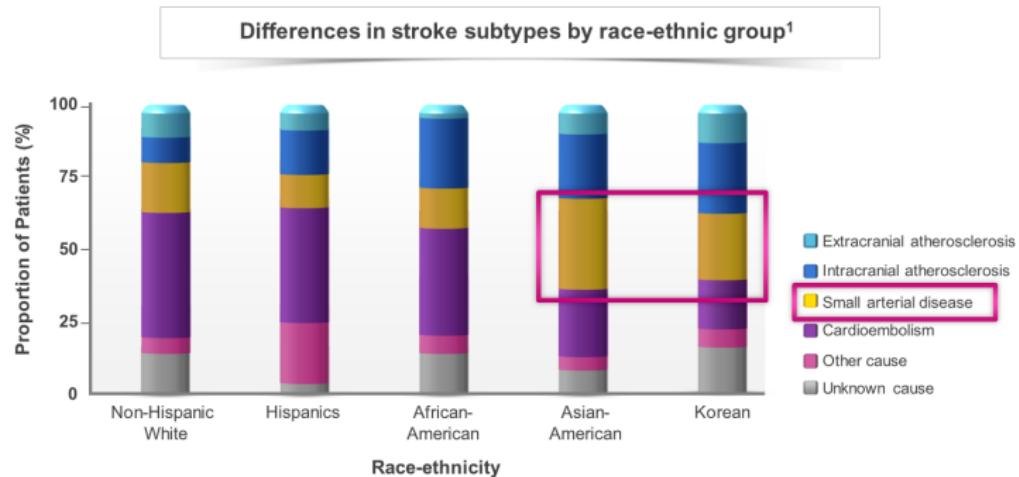
Lancet Neurol. 2014 383(9913): 245–254.

Age-standardised incidence of haemorrhagic stroke per 100 000 person-years for 2010



Lancet Glob Health. 2013 Nov; 1(5): e259–e281.

SVD is more prevalent in Asians than Western populations



Data collected over 4 yr-period in prospectively maintained registries on 3,053 subjects with ischemic cerebrovascular events (1,982 South Korean & 1,071 Southern California).

1. Bang OY, et al. Cerebrovasc Dis 2009;27:13–21. 2. Kim BJ, et al. J Stroke 2014;16:8–17.

RESEARCH ARTICLE

Genetic Variation at 16q24.2 Is Associated With Small Vessel Stroke

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Jordana T. Bell,¹¹ Eilis Hannon,¹² Jonathan Mill,^{12,13} Ganesh Chauhan,^{14,15}

Taylor M et al. Ann Neurol 2017

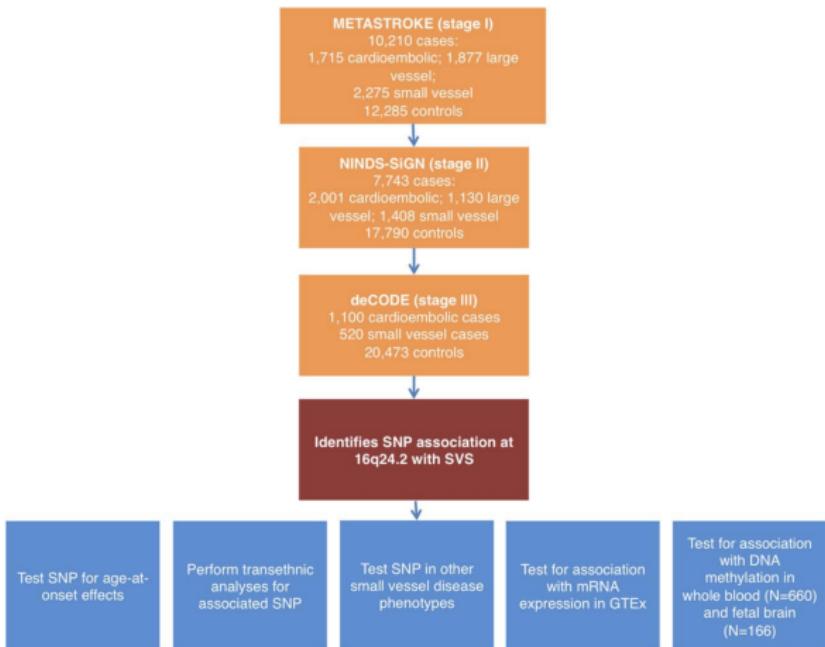


FIGURE 1: Flow chart of analyses performed. GTEx = Genotype-Tissue Expression; mRNA = messenger RNA; SNP = single-nucleotide polymorphism; SVS = small vessel stroke; [Color figure can be viewed at wileyonlinelibrary.com]

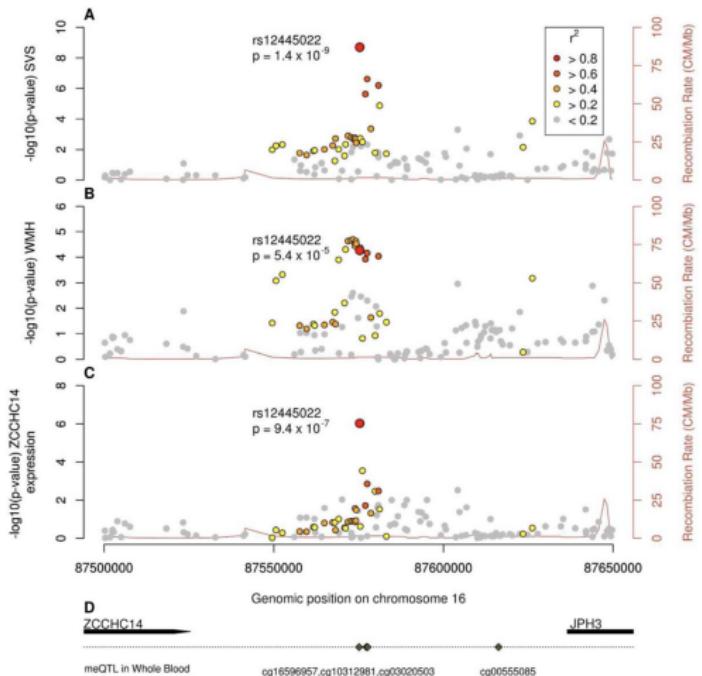


FIGURE 2: Associations at 16q24.2 with (A) small vessel stroke, (B) cerebral white matter hyperintensities, (C) mRNA expression of ZCCHC14, and (D) gene locations and associations of the locus with DNA methylation. mRNA = messenger RNA; SVS = small vessel stroke; WMH = white matter hyperintensities; ZCCHC14 = zinc finger CCHC domain-containing 14; JPH3 = junctophilin 3; meQTL = methylation quantitative trait locus. [Color figure can be viewed at wileyonlinelibrary.com]

IGSR and the 1000 Genomes Project

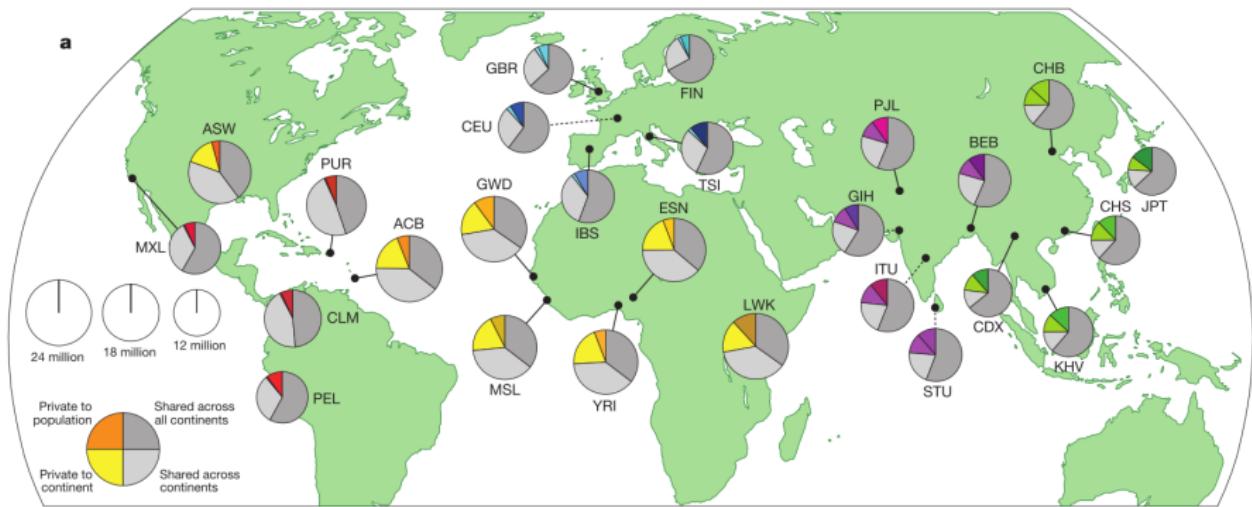


Populations: ● - African; ● - American; ● - East Asian; ● - European; ● - South Asian;

2,504 individuals from 26 populations

<http://www.internationalgenome.org/>

A global reference for human genetic variation



The 1000 Genomes Project. Nature 2015

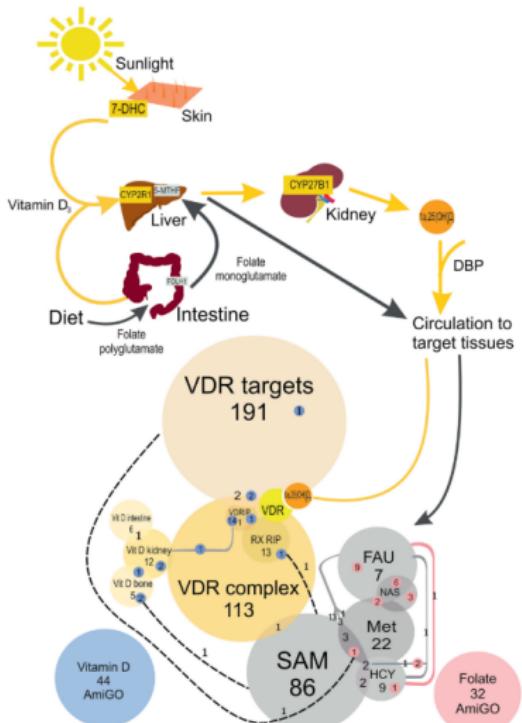
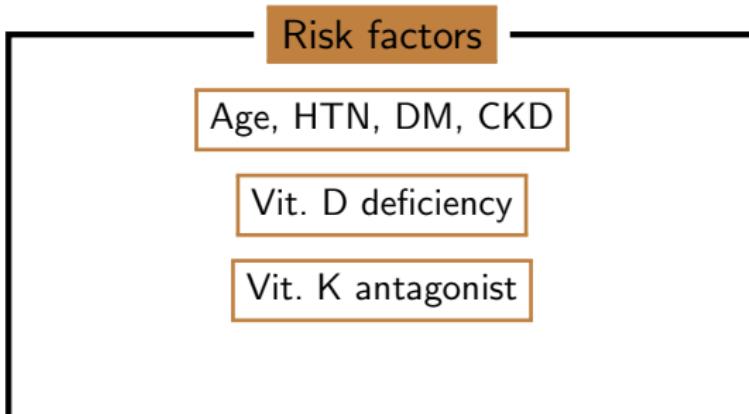


Fig 1. Vitamin D and folate acquisition, metabolism and gene sets analyzed in this study. The upper part shows metabolism of vitamin D (yellow)



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Vascular calcification

Arterial stiffness

Increased pulse pressure

CV morbidity and mortality

이광호교수님,

베풀어주신 은혜에 진심으로 감사드립니다.

항상 건강하시고 평안하시기를 기원드립니다.