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

Ischaemic stroke

20%
- Large-artery atherosclerosis
  - Extracranial ~12% (including aortic arch)
  - Intracranial ~8%
  - Haemodynamic failure with borderzone infarction (rare; not shown)
  - Artery-to-artery embolism or autochthonous atherothrombosis (common)

20–25%
- Cardiac disease
  - Atrial fibrillation
  - Ventricular thrombi
  - Valve disease
  - Reduced ventricular contractility
  - Cardiogenic embolism

20–25%
- Small-artery disease
  - Penetrating artery occlusion due to Lipohyalinosis
  - Atherosclerosis
  - Lacunar infarction (Leukoaraiosis)

5%
- Other causes
  - Dissection
  - Hypercoagulability
  - Vasculitis
  - Migrainous stroke
  - Drug abuse

25–30%
- Cryptogenic stroke
  - Various mechanisms of infarction
  - Various infarct morphology

A B C D E
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

- Components of cerebral small vessel disease
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Associations between SBP and risk of stroke

Asia Pacific Cohort Studies Collaboration

Prospective Studies Collaboration

Hazard ratio and 95% CI

Usual systolic blood pressure (mmHg)

Stroke 2004;35:1024
Pulse pressure and risk of stroke & WMLs

**Stroke**

**White matter lesions**

- 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
  - 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

- Transient falls in CBF during periods of lower BP

![Diagram showing autoregulation of CBF maintained despite change in CPP](image)
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


*Hypertension* 2008;52::1120
Increased Aortic Pulse Wave Velocity Is Associated With Silent Cerebral Small-Vessel Disease in Hypertensive Patients


(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

- **Pulse wave velocity** (Large artery stiffness)
- **Pulsatile Index** (microvascular stiffness)
- **Grading of CSVD**

**Key Structures**
- **Elastic Arteries**
- **Capillaries**
- **Venules**
- **Conductance Vessels**
- **Capacitance Vessels**
- **Arterioles**

**Images**
- Brain MRI scans
- Illustration of the cardiovascular system focusing on the aorta and its branches.
Arterial stiffness, PIs and severity of CSVD

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

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>β coefficient</th>
<th>t value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.008</td>
<td>4.659</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex</td>
<td>0.051</td>
<td>1.583</td>
<td>0.116</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>0.001</td>
<td>0.866</td>
<td>0.388</td>
</tr>
<tr>
<td>Heart rate</td>
<td>-0.001</td>
<td>-0.935</td>
<td>0.352</td>
</tr>
<tr>
<td>BaPWV</td>
<td>0.001</td>
<td>2.730</td>
<td>0.007</td>
</tr>
</tbody>
</table>

BaPWV = Brachial ankle pulse wave velocity; adjusted R² = 0.379.

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

<table>
<thead>
<tr>
<th></th>
<th>Multiple lacunes</th>
<th>Moderate to severe white matter lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Age</td>
<td>1.06 (1.01–1.12)</td>
<td>0.016</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.61 (0.22–1.67)</td>
<td>0.340</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.54 (0.99–6.53)</td>
<td>0.052</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.51 (0.18–1.40)</td>
<td>0.196</td>
</tr>
<tr>
<td>BaPWV (100 cm/increment)</td>
<td>1.21 (1.02–1.44)</td>
<td>0.028</td>
</tr>
<tr>
<td>Initial systolic BP</td>
<td>1.00 (0.98–1.02)</td>
<td>0.478</td>
</tr>
<tr>
<td>Heart rate</td>
<td>1.00 (0.95–1.05)</td>
<td>0.930</td>
</tr>
</tbody>
</table>

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

Aging

Vascular Risk Factors

Same biochemical & histological abnormalities in end-arteries

“Systemic Arteriolar Dysfunction” (Simultaneous SVD in multiple organs)

Brain
Lacunar infarctions, WM changes, Cognitive dysfunction

Kidney
Chronic kidney ds Subclinical renal failure

Eye
Retinopathy, Age-related macular degeneration

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

◆ Components of cerebral small vessel disease
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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**

<table>
<thead>
<tr>
<th>Incident WMH, n (%)</th>
<th>Total (n=192)</th>
<th>Placebo (n=103)</th>
<th>Active (n=89)</th>
<th>P Value, Model 1*</th>
<th>P Value, Model 2†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean volume of incident WMH, mm³ (SE)</td>
<td>1.8 (0.5)</td>
<td>2.0 (0.7)</td>
<td>0.4 (0.8)</td>
<td>0.012</td>
<td>0.009</td>
</tr>
<tr>
<td>Volume of incident WMH by initial grade of WMH, mm³ (SE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No WMH</td>
<td>0.05 (0.8)</td>
<td>0</td>
<td>0.09 (0.8)</td>
<td>0.76</td>
<td>0.81</td>
</tr>
<tr>
<td>Mild to moderate WMH</td>
<td>1.2 (1.2)</td>
<td>1.3 (1.0)</td>
<td>0.9 (1.0)</td>
<td>0.58</td>
<td>0.71</td>
</tr>
<tr>
<td>Severe WMH</td>
<td>6.5 (2.0)</td>
<td>7.6 (1.0)</td>
<td>0</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

_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.
감사합니다