A Novel Chronic Cerebral Hypoperfusion Model with Cognitive Impairment and Low Mortality Rate in Rats

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OBJECTIVE The cognitive deficit of vascular dementia (VD) and vasoocclusive state of moyamoya disease have often been mimicked with bilateral stenosis/occlusion of common/internal carotid artery. However, the cerebral blood flow (CBF) declines abruptly in these models after ligation of common carotid arteries (CCAs), which differs from “chronic” cerebral hypoperfusion. Thus, we developed a new chronic cerebral hypoperfusion (CCH) model.

METHODS We subjected male Sprague-Dawley rats to one-sided occlusion and contralateral side stenosis of the CCA (modified CCA occlusion [mCCAO]) and measured the cortical regional CBF (rCBF) using laser speckle flowmetry. Two groups mCCAO or sham operation assigned, we assessed their cognitive function and evaluated their cervical/intracranial arteries and the parenchymal injury with magnetic resonance imaging (MRI) after 4 weeks. Then, we histologically evaluated the rat brains.

RESULTS The mCCAO group revealed a gradual CBF reduction with a low mortality rate (2.3%). We observed white matter (WM) degeneration in the corpus callosum and corpus striatum. While the Cellular density declined in the hippocampus, MRI revealed no cerebral infarctions after mCCAO. Immunohistochemistry revealed upregulated inflammatory cells and angiogenesis in the hippocampus and cerebral cortex. Moreover, spatial learning and memory impairment were significantly high in the mCCAO group. The 8-week WM demonstrated some regeneration approaching sham animals.

CONCLUSIONS Our novel CCH model in rats using mCCAO is straightforward, with a low mortality rate, and could potentially investigate VD, moyamoya disease, and CCH, as well as the pathology of angiogenesis. This model was verified for an extended time-point of 8 weeks after surgery.
Shrinkage of Posterior Cerebral Artery involved in Moyamoya Disease - A Quantitative 3D-CISS Analysis

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Object - The involved arteries in carotid fork specifically decrease not only their own luminal calibers but also outer diameters in moyamoya disease (MMD). This study was aimed to clarify the changes in outer diameter of posterior cerebral artery (PCA) in MMD.

Methods - This study included 24 pediatric and 48 adult patients with MMD. Based on the findings on MR angiography, the degree of PCA involvement was classified into three grades: Grade 0, normal; Grade 1, stenosis; and Grade 2, occlusion. Using three-dimensional constructive interference in steady state (3D-CISS), the outer diameters were quantified in the P1 and P2 segments.

Results - The outer diameter of PCA decreased with a stepwise fashion as the stenotic lesion advanced in both P1 and P2 segments, and in both pediatric and adult patients. This phenomenon was more prominent in the P2 segment than in the P1 segment. In pediatric patients, the outer diameter of P2 segment was 2.00 ± 0.26 mm in Grade 0, 1.51 ± 0.42 mm in Grade 1, and 0.87 ± 0.15 mm in Grade 2 (P<0.001). In adult patients, the outer diameters of P2 segments were 2.03 ± 0.34 mm in Grade 0, 1.48 ± 0.34 mm in Grade 1, and 1.07 ± 0.17 mm in Grade 2 (P<0.001).

Conclusion - This study demonstrates that MMD also leads to specific shrinkage in the PCA. This phenomenon is more prominent in the P2 segment, suggesting the involvement of development factor in pathogenesis of MMD.
The efficiency of FLAIR images for hemodynamic change after STA-MCA bypass with Moyamoya disease and symptomatic steno-occlusive disease

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Purpose: Hyperintense vessels (HV), representative of leptomeningeal vessels on FLAIR were assumed to be explained by slow antegrade or retrograde leptomeningeal collateral flow related to steno-occlusion. We investigated the correlation between HV and cerebral vascular hemodynamic status and the effect of recanalization after STA-MCA bypass of in patients with Moyamoya disease and symptomatic steno-occlusive disease. Methods: forty-nine patients with Moyamoya disease and symptomatic steno-occlusion during 4 year who underwent pre- and postoperative FLAIR with STA-MCA bypass were retrospectively enrolled. The presence of HV on FLAIR was classified as Negative, Minimal and Positive. Regions were classified into four territories. Correlations between HV and hemodynamic status measured by SPECT and perfusion MRI were evaluated. The relationship between changes of the HV was examined in affected hemisphere of each patient after successful treatment with bypass. Result: The presence of HV was seen on affected hemispheres in 36 of 49 patients (74%). In SPECT, CVR in the areas with positive or minimal HV was lower than that in the areas with negative. With follow-up FLAIR after 3 to 14 month after bypass, HV decreased or disappeared in 32 (65%). CVR on SPECT and perfusion MRI also demonstrated apparent hemodynamic improvement in same areas. Conclusions: HV is related to leptomeningeal collateral flow with Moyamoya and steno-occlusion disease and the HV-positive hemisphere shows a lower vascular. This study indicates that STA-MCA bypass was effective for hemodynamic improvement and decreasing HV and postoperative decrease in HV on FLAIR can be considered as useful marker for hemodynamic improvement.
Long-term outcome of intravenous thrombolysis for acute ischemic stroke

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Although intravenous thrombolysis (IVT) using recombinant tissue plasminogen activator is a primary treatment for acute ischemic stroke (AIS), it is still debated whether or not IVT could reduce the mortality during long-term follow-up. As IVT has a very restricted inclusion criteria, eligible patients for IVT are very small. And long-term prognosis for the patients who had contraindication to IVT is unclear. So, using Health Insurance Review & Assessment Service database, we evaluated the long-term prognosis between IVT group and contraindication group of IVT.

A total of 4380 subjects were selected from a total of 169 medical institutions in South Korea during 2011, 2013. 1,027 (19%) patients who received the IVT within 4.5 hours after onset. Total 3,686 patients did not received the IVT because of contraindication of IVT. Oh these, 3,378 (77.1%) patients were admitted over 4.5 hours, and 144(3.3%) patients had unknown time of stroke-onset. 53(1.2%) patients had the condition of non-adjustable hypertension or bleeding diathesis. 137(3.1%) patients had rapid improvement or mild stroke in hospital. Compared with IVT group, the patients who did not receive IVT because of time-restriction and rapid improvement or mild stroke in hospital had lower survival rate during 5-years. And the patients who did not received IVT because of non-adjustable hypertension or bleeding diathesis had lowest survival rate during long-term follow-up (log-rank p<.001).

IVT have a powerful effect to improve the survive during long-term follow-up. And some contraindication of IVT should be re-evaluated or substituted the other bridging therapy to reduce poor long-term prognosis on AIS.
Outcome of superficial temporal artery to middle cerebral artery anastomosis in acute period of cerebral infarction

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Purpose
The authors performed urgent superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis in acute period for the patients who was in progressive stroke or failed to fibrinolytic therapy. We investigated the effect of bypass surgery in acute period and good prognostic factors.

Method
A total of 83 patients who presented with large cerebral artery occlusion and underwent emergency STA-MCA anastomosis were enrolled in this study for 9 years. Diffusion/perfusion Magnetic Resonance Image (MRI) and catheter angiography findings are major determinants of decision making of surgery. Only the patient who had small volume of infarction (less than 30cc) and large volume of perfusion defect with MRI study was selected as a surgery candidate.

Results
Initial national institute of health stroke scale (NIHSS) was 2 to 22. Mean volume of infarction was 8.3cc and mean time to peak (TTP) delay area volume was 75cc. NIHSS was higher in perforator infarction group (9.4 vs 3.6). There was no case of post-operation intracerebral hemorrhage or mortality. Post operative perfusion MRI at 1 week revealed full recovery of TTP delay in almost cases. Surgical outcomes according to modified Rankin score (mRS) are as follow respectively ( IV:9,III:11,II:19,I:18,0:27)

Conclusion
Small infarction volume in the watershed area with large perfusion defect can be a good candidate for bypass surgery. It can improve the blood flow in critical area with little risk of reperfusion injury because of low flow characteristics. Bypass surgery in acute period of infarction can be a good option because it has a considerable long time window.