FPⅢ-1

Critical Role of PDGFR-α in Angiogenesis through Indirect Bypass in Mouse Model of Moyamoya Disease

Tomohide Hayashi

Departments of Neurosurgery, University of Toyama

Background - Moyamoya disease is a unique cerebrovascular disorder with unknown causes. The mechanism of angiogenesis via indirect bypass surgery in moyamoya disease also remains obscure. In this study, we established a mouse moyamoya disease model, performed encephalo-myo-synangiosis (EMS), and evaluated the role of platelet-derived growth factor (PDGF) in a distinct angiogenesis in moyamoya disease.

Methods - Using 8-week-old Flox and PDGFR-α knocked out (α-KO) mice, the common carotid artery stenosis (BCAS) was produced. They underwent (EMS) on the right side one week after BCAS. Cerebral blood flow (CBF) was serially measured with a laser Doppler flowmeter. The brain tissue was transcardially perfused and harvested 30 days after BCAS. The specimens were subjected to Klüver-Barrera staining and Sirius red staining. Immunohistochemistry against CD31 was also performed.

Results - CBF was reduced to 35% of the control just after BCAS, and improved to 70% after 30 days post-BCAS. There was no difference between Flox and α-KO mice. EMS significantly improved CBF on the ipsilateral side in the Flox mice, but not in α-KO mice. Histological analysis revealed the dilation of cortical vessels besides EMS and the accumulation of collagen between the cortex and temporal muscle in the Flox mice, but not in α-KO mice.

Conclusion - PDGFR-α may play an essential role to promote angiogenesis via indirect bypass in moyamoya disease.
Geometrical complexity of cortical microvascularization in moyamoya disease

Katsuya Komatsu¹, Takeshi Mikami², Yukinori Akiyama², Rei Enatsu², Hime Suzuki², Masahiko Wanibuchi², Nobuhiro Mikuni²

¹Department of Neurosurgery, Sapporo City General Hospital / Department of Neurosurgery, Sapporo Medical University
²Department of Neurosurgery, Sapporo Medical University

BACKGROUND: Dilatation of the microvascular diameter is recognized in moyamoya disease (MD), and referred to as microvascularization. The purpose of this study is to characterize the cortical microvascularization in MD using imaging analysis, and to explore the developmental mechanism of the collateral network around the cortical surface.

METHODS: A total of 20 hemispheric sides of 14 patients with MD were included. From the intraoperative images, cortical surface images were extracted, and binary images were subsequently created. Then the ratio of the microvessels of the brain surface (vascular fraction; VF) and the box-counting fractal dimension (Db) values were calculated. The VF and Db values in the MD group were then compared with those in atherosclerotic disease (ASD) and non-ischemic disease (NID) group, and assessed in terms of clinical and radiologic factors.

RESULTS: VF was significantly higher in the MD group compared with the ASD group, and Db was significantly higher in the MD group compared with the ASD and NID groups. In MD, VF showed moderate correlation with magnetic resonance angiography (MRA) score. Moreover, Db was significantly higher in the pediatric patients, in the presence of ischemic symptoms, and in the presence of ivy sign, and Db showed a moderate correlation with MRA score and cerebral blood flow in moyamoya disease.

CONCLUSIONS: In the patients with MD, the cortical microvascularization exhibited increased Db and dilatation of the pial arteries. In MD, cortical microvascularization is associated with clinical and radiologic factors. This microvascularization might be a compensatory mechanism in the ischemic condition in MD.
FPⅢ-3

Extracranial systemic arteriopathy in adults with moyamoya disease: a prospective study

Tae Keun Jee, Jong-Soo Kim, Seung-Chyul Hong, Je Young Yeon

Samsung Medical Center

Background: The association of moyamoya disease (MMD) with extracranial systemic arteriopathy such as coronary, celiac, mesenteric and/or renal artery stenosis has been rarely reported in the literature. The main purpose of this study was to determine the prevalence of extracranial arteriopathy in adults with moyamoya disease. Methods: We prospectively enrolled 58 adults aged 20 - 50 years and recently diagnosed to have MMD based on typical angiographic findings. Patients with known cardiac, renal, or systemic vascular diseases were excluded. Coronary-aorta CT angiography was performed for the presence of steno-occlusive lesions in the coronary and major thoracoabdominal arteries. Clinical characteristics including risk factors of atherosclerosis were collected and direct sequencing of exon 60 of the RNF213 gene was performed for the presence of the rs112735431 variant (c.14429G>A, p.R4810K).

Results: Fourteen of the 58 patient (24.1%) were found to have coronary artery stenosis, that was moderate (>30%) in 5 patients. Eleven patients (19.0%) exhibited concurrent stenosis in the celiac or mesenteric artery. Renal artery stenosis was identified in 2 (3.4%) and associated with hypertension. The rs112735431 variant was identified in 44 of the 58 patients (75.9%), and 3 of them had homozygote mutation.

Conclusions: Extracranial systemic arteriopathy is not uncommon in adults with MMD and presumed to be non-atherosclerotic in many of them. Systemic vascular evaluation may be warranted in MMD patients although it remains to be determined whether this co-occurrence represents a common vascular pathology.
FPⅢ-4

Postoperative angiogram factor and neurological outcome assessment of pediatric MMD patients

Masataka Hayashi¹, Akitsugu Kawashima¹, Yoshichika Kikuta¹, Kazutoshi Hashimoto¹, Ayumi Nagahara¹, Takashi Arai¹, Akikazu Nakamura¹, Takakazu Kawamata²

¹Tokyo Women's Medical University Yachiyo medical center
²Tokyo Women's Medical University

(Background) Pediatric MMD is rare, so it is not so clear that postoperative angiogram is associated with neurological outcome. (Purpose) This time, we assessed the relevance of postoperative 6 months direct bypass development and prevention of TIA or any stroke. (Method) Pediatric case was defined as under 15 years old. In Apr.2013 - Jul. 2017, operated 40 sides, pediatric patients (32 sides was STA-MCA double bypass, 8 sides was OA-MCA) Indirect bypass was added under 8 year patients. Postoperative 6 months later, was taken angiogram, SPECT, MRI. The investigation points were pre and post-operative angiogram factor (PCA involvement, ECA/ICA dilation ratio, STA or OA/ICA ratio, territory of direct bypass), And we studied statistically two groups as TIA group and non-TIA group with SPSS22. (Result) Mean Age 7.06±2.05, female was 18, non TIA group was 27 sides. These angiogram factor was significant differences between two group, (Preoperative ECA/ICA dilation ratio, p=0.05 Postoperative STA or OA/ICA ratio, p=0.021 Area of direct and indirect bypass p=0.029 ) (Consideration and Conclusion) Preoperative ECA/ICA ratio was considered, direct and indirect potential. In the same idea, adequate development of direct/indirect bypass was showed bypass area and postoperative STA or OA/ICA ratio. It may be clear that the good development of bypass causes the prevention of TIA or Stroke.
The Efficacy of Single Barrel Superficial Temporal Artery-Middle Cerebral Artery Bypass in Treatment of Ischemic-type Adult Moyamoya Disease

Jun Kyeung Ko¹, Chang Hwa Choi¹, Sang Weon Lee²

¹Department of Neurosurgery, Pusan National University Hospital
²Department of Neurosurgery, Pusan National University Yangsan Hospital

Objective: So far, there is no study answering the question of which type of surgical technique is practically the most useful in the treatment of adult patients with ischemic type moyamoya disease (MMD). We evaluated the efficacy of single barrel superficial temporal artery (STA)-middle cerebral artery (MCA) bypass in the treatment of these patients by retrospectively collecting clinical and radiological data.

Methods: A retrospective review identified 31 adult patients who underwent 43 single barrel STA-MCA bypass procedures performed for treatment of ischemic-type MMD between 2006 and 2014. No other indirect revascularization procedures were added during the surgery to reduce peri-operative morbidity.

Results: The permanent neurological morbidity and mortality rates were 2.3% and 0%, respectively. During the observation period of a mean of 35 months (range, 12-73 months), 29 patients (93.5%) had no further cerebrovascular events and TIA occurred in two patients (6.5%), resulting in an annual stroke risk of 2.2%. Follow-up computed tomography perfusion (CTP) (mean, 18.4 months after surgery) documented improved cerebral hemodynamics in the revascularized hemispheres (p <0.001). Post-operative patency was clearly verified in 38 bypasses (88.4%) of 43 bypasses on follow-up imaging (mean, 16.5 months).

Conclusion: Our results suggest that single barrel STA-MCA bypass without additional indirect revascularization procedures is safe and durable method of cerebral revascularization in adult patients with ischemic type MMD and can be considered as a potential treatment option for these patients.
FPⅢ-6

**Acute thrombogenesis just after bypass procedure in moyamoya disease**

Takeshi Mikami, Hime Suzuki, Ryo Ukai, Katsuya Komatsu, Nobuhiro Mikuni

*Sapporo Medical University*

**BACKGROUND** Extracranial-to-intracranial (EC-IC) bypass surgery is an effective treatment strategy for patients with moyamoya disease and other conditions. There is a potential risk of acute thrombogenesis just after bypass surgery in some cases, and this is especially true in cases of moyamoya disease. In this study, we report the risk factors of acute thrombogenesis and discuss our countermeasures against acute thrombogenesis in EC-IC bypass.

**METHODS** This study included 96 patients (45 with moyamoya disease and 51 non-moyamoya disease controls [aneurysm, atherosclerotic disease, and brain tumor]) who underwent 118 EC-IC bypass procedures. The appearance of acute thrombogenesis was compared between the moyamoya disease group and the control group. Clinical and radiological characteristics were then compared between the group of moyamoya disease patients in which acute thrombogenesis occurred and the group in which it did not.

**RESULTS** The incidence of acute thrombogenesis was significantly higher in the moyamoya disease group than in the control group. The predictive factors that were associated with acute thrombogenesis in the patients with moyamoya disease using multivariate analysis were higher prevalence of hemorrhagic stroke onset (Odds ratio, 6.803; p = 0.029) and higher MRA scores (Odds ratio, 2.354; p = 0.010).

**CONCLUSIONS** During EC-IC bypass surgery in moyamoya disease, acute thrombogenesis should be taken into consideration, especially in cases with hemorrhagic stroke onset and a high MRA score for obtaining a high patency rate. This acute thrombogenesis will not influence morbidity if proper countermeasures are employed; therefore, prediction and recognition of white thrombi is important.
Long-term physical and social prognosis of pediatric moyamoya disease treated by direct bypass surgery

Eika Hamano¹, Masaki Nishimura¹, Tetsu Satow¹, Takashi Funaki², Koji Iihara³, Susumu Miyamoto², Jun Takahashi¹

¹Department of Neurosurgery, National Cerebral and Cardiovascular Center
²Department of Neurosurgery, Kyoto University Hospital
³Department of Neurosurgery, Graduate School of Medical Sciences Kyushu University

<Purpose>Many reports have revealed that bypass surgery for pediatric moyamoya disease contribute to good physical prognosis. There are, however, few reports regarding the long-term social outcomes after growing up. We report the result of retrospective analyses of the medium to long-term physical and social prognosis after bypass surgery in pediatric moyamoya disease.

<Methods>95 children (≤ 15 y) with 182 affected hemispheres underwent surgical intervention during 1998 and 2011 in our institute. The mean follow-up period was 8.9 ± 3.7 years. STA-MCA single bypass with EMS were performed as a standard surgical technique, and additional bypass procedures targeted the ACA or PCA territories were performed only in the selected patients thereafter. We investigated the following items:1) Occurrence of cerebrovascular events, 2) frequency of TIA, 3) status of school enrollment and employment. Unfavorable social outcome was defined as difficulty in attending regular school or inability to obtain regular employment.

<Result>One patient suffered intracranial hemorrhage at age of 19 (13 years after surgery). No Cerebral infarction was observed. Additional bypass surgery was performed in 23 cases (24.2%). Poor physical outcome (mRS3-5) was observed in 3 cases at the time of the last follow-up, all of which were attributed to cerebral infarction at the initial onset. Unfavorable social outcome was observed in 6 cases, among which 5 cases were judged as having good physical outcome (mRS 0-2).

<Conclusion>De-novo neurological events are rare after bypass surgery. It should be emphasized that good physical outcome does NOT always indicate the good social outcome.