Delayed intracranial parenchymal changes after aneurysmal coil embolization procedure.

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[Background] With recent advancement of endovascular techniques and devices, coil embolization for unruptured cerebral aneurysms has been mundanely performed, however, delayed complications caused by several devices for endovascular procedures has been described. In the present study, we investigated the characteristics, pathology and treatment of the delayed intracranial parenchymal changes after aneurysmal coil embolization procedures.

[Methods] From 2015 to 2017, 305 patients who underwent coil embolization for cerebral unruptured aneurysms at our related institutes were included. Delayed intracranial parenchymal changes were defined as late-onset symptomatic inflammatory changes which showed multiple cerebral white matter lesions that coincided with the target vessel perfusion territories and resolved by steroid administration.

[Results] Seven cases (2.3%) showed late-onset symptomatic inflammatory changes after the procedures, and six out of seven cases underwent stent-assisted coil embolization. In 2 cases, nickel allergy was proved by the skin patch test.

[Discussion] As causes of delayed inflammatory parenchymal changes after endovascular coil embolization, contrast agent encephalopathy, coil compression, PRES, metal allergy, foreign body allergy may be considered. In our series, 2 cases which proved nickel allergy, suggesting the possibility of nickel allergy. With respect to the other 5 cases, it was also possible that inflammatory changes such as metal allergy or coating polymer peeled off from the catheter during procedures.

[Conclusion] In performing aneurysmal coil embolization procedures, it is necessary to fully recognize that there are possibilities of delayed inflammatory changes due to the use of various devices.
SYII-2

Long-term functional outcomes of unruptured intracranial aneurysms using retrospective propensity score-matched cohort analysis

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Objective
Total management of unruptured intracranial aneurysms (UIAs) remains controversial. We sought to clarify the effectiveness of our comprehensive management to keep activities of daily living (ADL) of patients with UIAs during follow-up.

Materials and Methods
A retrospective analysis was performed in consecutive 408 patients with at least one saccular UIA (≥2 mm in size) and followed from April 2007 through December 2016. ADL decline was defined as deterioration of modified Rankin Scale from 0-2 to 3-6 and the primary outcome. The secondary outcomes included rupture of IA and death. We compared outcomes between non-intervention group and intervention group. Association between outcomes and intervention was statistically analyzed using propensity score-matched (PSM) cohort.

Results
Finally 346 patients were enrolled. Median follow-up time was 63.5 months (range: 2 to 193). Mean age (±SD) was 65.9 ±11.3 years. 46 ADL declines were observed (37 vs 9 between non-intervention group and intervention group). Major causes of ADL decline were 9 cancers, 5 aneurysmal ruptures, 5 strokes and others. 8 aneurysmal ruptures (8 vs 0) and 24 deaths (20 vs 4) were observed with an annual rupture of 0.43% and an annual mortality of 1.3%. Associations of intervention with ADL decline, rupture and death were analyzed by Cox regression model in PSM cohort (HR=0.48, P=0.093; HR=NA, P<0.0001; HR=0.36, P=0.13). Intervention significantly suppressed ADL decline in patients with aneurysm >5mm in size in the cohort (HR=0.24, P=0.028).

Conclusion
ADL decline of patients with UIA during follow-up could be avoided by comprehensive management including intervention and observation.
Large cerebral aneurysms have been hard to cure still now. We treated large internal carotid artery aneurysms by bypass and trapping till 2009. Then, we changed a strategy to coil embolization with stent in 2010. Finally, we have treated them by flow diverter stent from 2015. I present 10 cases of bypass and trapping, 35 cases of coil embolization, and 50 cases of flow diverter stent. Although the result of bypass and trapping were excellent, flow diverter stent is a promising device for large aneurysms now. I show our result and discuss about complications and outcome. In Japan, endovascular therapy has been performed by neurosurgeons. So, treatment strategy for aneurysms is depended on each department. In our department, 80% aneurysms were treated by endovascular therapy. The public opinion tends to avoid invasive treatment. We have to indicate the most suitable treatment for each patients independently on personal experience of neurosurgeons. However, any guidelines never cover all aneurysms. We should select the best treatment with the times.
Altered trend in background and treatment modality in the patients with ruptured cerebral aneurysm during the last decade

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With the aging of society and progress of intravascular treatment, we reconsidered the roles of craniotomy for the patients with subarachnoid hemorrhage (SAH) due to ruptured cerebral aneurysm.

Materials and methods: We experienced 512 patients with SAH in last 10 years; age 29-96 year-old, 151 male 361 female. We examined their severity, treatment, outcome, complications, etc. in all cases and radical treatment cases (467). The patients was divided into the first (2007-11; 245) and the second period (2012-16; 267). Craniotomy was the first line in the first period, but indication of endovascular treatment has been expanded in the second period.

Results: In 10 years, significant progress of aging has been observed. Although the distribution of disease severity does not change, the proportion of patients with existing disabilities and general complications increased significantly. In multivariate analysis, age, cerebral infarction due to cerebral vasospasm, disease severity, existing disability and general complication were predictors of poor outcome (modified Rankin scale 3-6). Patients treated with endovascular treatment increased from 6.5% to 20%. The frequency of surgical complications was around 25%, being not significantly different between each modality. Overall ratio of poor outcome have not changed at all. The outcome is well maintained regardless of aging, because patients with accompanied complications are mainly treated by endovascular manner.

Conclusions: The role of endovascular treatment for SAH is increasing. Safety as well as robustness should be taking into account when we consider which treatment should be selected for the particular aneurysm.
According to the guideline of AHA, for patients with ruptured aneurysms judged to be technically amenable to both endovascular coiling (EC) and neurosurgical clipping (SC), EC should be considered. However, there have been some papers reported with different results. Now, we compared the outcome after SC with after EC for the patients with aneurysmal subarachnoid hemorrhage (aSAH) using the big database in Japan. The stroke data bank in Japan with 3593 cases of aSAH showed that no significant differences in modified Rankin scale (mRS) at discharge were found between SC and EC (p=0.22) and that the cutoff age of ROC analysis for poor mRS > 2 was 3 to 9 years older by EC than SC. The Diagnosis Procedure Combination (DPC) database in Japan showed that the propensity score-matched analysis of 3,561 non-elderly patients (< 65 years) showed no significant difference for poor outcome between SC and EC (34.3% vs 32.9%, p=0.19; risk difference -1.5%), however 3,559 elderly patients (≧ 65 years) undergoing SC showed significantly higher rates of poor outcome (65.5% vs 61.34%, p=0.002; risk difference 4.3%) compared to EC. In-hospital mortality was significantly higher after EC than SC in both groups. ROC analysis for poor outcome of the total group showed the cut-off ages of 67.5 years for SC (AUC 0.70) and 71.5 years for EC (AUC 0.69). The treatment indication should be carefully considered based on the characteristics of the aneurysm and the patients with aSAH, especially in non-elderly individuals.
Results and current trends of cerebral aneurysm surgery

SYII-6

Outcomes of open procedures for unruptured intracranial aneurysms and prediction model - implications from the UCAS Japan cohort

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Background: Management strategy of the unruptured intracranial aneurysms (UIA) should be made by balancing rupture risk and management risk of aneurysms as well as patient’s physical and mental conditions. Rupture risks and its prediction models of UCA have been recently reported, but management risks need to be further clarified. We now report the treatment data from a Japanese cohort and created risk prediction model in conjunction with rupture risks in this cohort.

Method: In the cohort of UCAS Japan, 2,316 underwent open craniotomy. Morbidity was defined as decline of modified Rankin scale to the level of two or below at one month after treatment. Factors with p value less than 0.10 by multivariate cox regression model were considered important and included in the prediction model for management morbidity. Prediction scores were derived from multivariate hazard ratio.

Results: Overall morbidity was recorded in 65 cases (2.8%). Important risk factors were as follows; Size $\geq$ 10mm, Basilar Location, not associated with daughter sac, Age $\geq$ 70, Hypertension, Diabetes Mellitus, initial modified Rankin scale and multiple aneurysm treatment at one cession. Neither hospital treatment volume nor method of treatment affected treatment morbidity. We created risk prediction model for morbidity to be balanced with rupture prediction score.

Conclusions: Risks associated with management of UIA can be stratified with several factors. Risk prediction model of management as shown here should support decision making on UIA management in conjunction with rupture risk prediction model.
The History and Update of Cerebral Aneurysm Management

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The great pioneers of aneurysm surgery in the mid and late 20th century had made a lot of effort to lay foundation for basic concept and technique for aneurysm microsurgery. The advancement of microsurgical techniques by many great vascular neurosurgeons, such as Dr. Drake and Dr. Yasargil, and development of neuroradiology and surgical equipment allowed the tremendous improvement of treatment results of aneurysm microsurgery. In addition to direct neck clipping, coil embolization introduced by Dr. Guglielmi in 1991, has represented as effective solution for most saccular aneurysms especially in posterior circulation, and number of coil embolization has increased in relation to neck clipping as years passed. Since the years 2006-2007, a new generation of neurovascular stent, flow diverter device, such as Pipeline Embolization Device (PED), can exclude the sac from circulation in fusiform, dissecting, large, giant and wide necked aneurysm.

Subarachnoid hemorrhage (SAH) due to ruptured aneurysm is still very hazardous and dangerous disease, because of its high mortality and morbidity rates even in 21st century with marked improvement of management of SAH. Prevalence of saccular intracranial aneurysm is around 1% in population and incidence of SAH gives figures around 10/100,000 people/year. Therefore, unruptured aneurysm has a risk of bleeding of 1%/year, approximately. There has been a lot of report about natural history of unruptured aneurysm, and some controversies still remained which aneurysm will be ruptured, especially in small sized aneurysm. The one of the best ways to prevent SAH is disturbing aneurysm formation and its growth by reducing the risk factors such as hypertension and cigarette smoking, and another way is to find the unruptured aneurysm by CTA and MRA and treat it before rupturing in good condition by neck clipping or endovascular coiling. According to our database of treatment for cerebral aneurysms during last 10 years, we found about 15% of ruptured aneurysms were very small aneurysms (VSAs) with size of under 3mm in diameter which had poor grade clinical condition on admission and outcome. Therefore, we treated VSAs actively even in unruptured cases by direct neck clipping or endovascular coiling with acceptable complication rate.
Maximize endogenous recovery after stroke with endovascular stem cell therapy

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Stem cell transplantation for stroke treatment has been a promising therapy in small and large animal models, and many clinical trials are ongoing to establish this strategy in a clinical setting. However, the mechanism underlying functional recovery after stem cell transplantation has not been fully established and there is still a need to determine the ideal subset of stem cells for such therapy. We herein reviewed the recent evidences showing the underlying mechanism of functional recovery after cell transplantation, focusing on endogenous brain repair. First, angiogenesis/neovascularization is promoted by trophic factors including vascular endothelial growth factor secreted from stem cells, and stem cells migrated to the lesion along with the vessels. Second, axonal sprouting, dendritic branching and synaptogenesis were enhanced altogether in the both ipsilateral and contralateral hemisphere remapping the pyramidal tract across the board. Taken together, it is clear that stem cell transplantation provides functional recovery via endogenous repair enhancement from multiple ways. This is important to maximize the effect of stem cell therapy after stroke, although it is still undetermined which repair mechanism is mostly contributed. We also review the potential of endovascular (intraarterial) delivery of stem cell for stroke.
The limitation of a current thrombolytic treatment for ischemic stroke leads to exploration of new therapeutic strategies targeting the restorative stage over the acute narrow therapeutic window, such as cell-based therapies. To develop the cell-based therapy, various donor cell types have been transplanted, such as adult stem cells, embryonic stem cells, and induced pluripotent stem cells, into injured sites of animal models. Although the transplantation of these cell types substantially promotes the functional recovery of stroke, there are several limitations that may impede its clinical application such as limited efficacy, risk of tumorigenesis, and ethical problems. We have explored and studied the methods to overcome these obstacles. For example, fibroblasts have been directly converted into induced neural stem cells (iNSCs) by the forced expression defined transcription factors. iNSCs could circumvent the pluripotent state and eliminate the risk of tumorigenesis. Meanwhile, hypoxic preconditioning of stem cells can enhance the cells’s therapeutic potential and it is currently employed as a strategy to prepare stem cells for increased survival and engraftment in the host. On the other hand, mannitol enhances blood-brain barrier permeabilization and mannitol can improves the efficiency of systemically administered stem cells by facilitating the entry of the stem cells from the periphery into the adult stroke brain. Here, based on these studies, we show our recent basic researches to improve therapeutic effect of stem cells for the ischemic stroke.