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VIRTUAL

PROGRAM BOOK

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Cardioembolic stroke has been one of the essential themes of our cerebrovascular team during the past 45 years after the inauguration of the National Cerebral and Cardiovascular Center (NCVC) in Osaka. In the pioneer days, my seniors did not have developed database or cutting-edge technological tools but had plenty of cardiac patients developing embolic tragedies. It was natural that they devoted their attention to pathophysiology and pathogenesis of cardioembolic stroke. My master, Dr. Yasaka, continued to monitor the growth of intraatrial thrombi repeatedly for acute cardioembolic patients and discovered several major scientific findings in his resident days. When I started my residency in NCVC in 1989, the master handed me a Lightsaber, an early form of a “monoplane” transesophageal echocardiography. The saber revealed the rearmost part of the left atrial appendage, providing me with fresh surprises and intellectual excitements. It was a beginning of my long brain-heart journey. Warfarin has been our powerful medicine and poison for pharmacotherapy of cardioembolism. Do you believe that the international normalized ratio of prothrombin time was seldom used in early 90’s? Can you imagine that cardioembolic patients were generally younger than atherothrombotic patients and their main embolic diseases were rheumatic heart disease and out-of-control infectious endocarditis in my resident days? Direct oral anticoagulants replaced warfarin for the last decade. I was lucky enough to form the multicenter registry of the SAMURAI-NVAF with my Japanese friends. The database was then merged with the database of the Clinical Research Collaboration for Stroke in Korea (CRCS-K) or with European datasets to explore best secondary stroke prevention. In recent years, nonpharmacological preventive strategies against stroke using cardiac devices have aroused my interest. As Prof Luciano Sposato introduces in this KJJSC 2022, the World Stroke Organization (WSO) built a new project named WSO-BEAT (Brain & Heart globe initiative) for global development of high-quality brain-heart collaboration. My journey continues.

**Journal of the American Heart Association**

**ORIGINAL RESEARCH**

Transesophageal Echocardiography in Ischemic Stroke With Atrial Fibrillation

Kanta Tanaka, MD, PhD; Masahiro Koga, MD, PhD; Yujiro Takahashi, MD, PhD; Kyoji Uesugi, MD, PhD; Yutaka Yaegashi, MD, PhD; Susumu Kato, MD, PhD; Takuro Takahashi, MD, PhD; and the CRCS-K Investigators

Atrial Fibrillation-Associated Ischemic Stroke Patients With Prior Anticoagulation Have Higher Risk for Recurrent Stroke

Kanta Tanaka, MD; Masahiro Koga, MD, PhD; Kyoji Uesugi, MD, PhD; Yutaka Yaegashi, MD, PhD; Susumu Kato, MD, PhD; Takuro Takahashi, MD, PhD; and the CRCS-K Investigators

Prediction of recurrent stroke among ischemic stroke patients with atrial fibrillation: Development and validation of a risk score model

Beom-Joon Kim, MD, PhD; Ji-Yeon Park, MD, PhD; and the CRCS-K Investigators

**PLOS ONE**

Works for CRCS-K & SAMURAI-NVAF

**Stroke**

For the CRCS-K Investigators and the SAMURAI Study Investigators
After success of five randomized controlled trials (RCTs), mechanical thrombectomy (MT) has become a standard treatment in hyperacute ischemic stroke due to large vessel occlusion in 2015. MT is increasing year after year in Korea. Performing MT at the earliest time possible increases the chance of a good prognosis for patients with acute ischemic stroke. To improve the patient’s prognosis, obtaining the successful reperfusion as early as possible is the key factor. Many efforts are being made toward a goal of early and complete recanalization. According to the evolution of the device, appropriate patient selection via multimodal brain imaging, the achievement of successful reperfusion is getting higher, and prognosis of the patients is more favorable. Also, there is a struggle for the efficient thrombectomy workflow, the timeline after the arrival of ischemic stroke patient is getting shorter. During MT, the evidence of using balloon guiding catheter is added. The techniques and novel device have been introduced in Korea. Several techniques used on difficult cases (tortuous vascular anatomy, refractory to MT, failure of femoral puncture, re-occlusion after an initial success of recanalization) are reported. Also, new stent-retrievers are available in Korea and newly developed stent-retriever is ready for use. For medical management after MT, RCTs are ongoing in Korea.
Stoke is the fourth leading cause of death in Japan, and cerebral infarction accounts for two-thirds of them. Mechanical thrombectomy (MT) is the most effective treatment for emergent cerebral large vessel occlusion. In 2019, the Basic Act on Measures against Stroke and Cardiovascular Disease was enacted, and the nationwide activity to spread MT was accelerated. To ensure safe treatment, operators of MT in Japan are limited to specialists in neuroendovascular therapy or thrombectomy capable practitioners authorized by Japanese society of NeuroEndovascular Therapy (JSNET), which has over 4,000 members. JSNET specialists have not only clinical experience with 100 cases of neuroendovascular treatment but also written and practical tests. Thrombectomy capable practitioners should have similar experiences but do not impose tests. Currently, there are 1748 JSNET specialists (90% neurosurgeons, 8% internal medicine) and 533 thrombectomy capable practitioners. In addition, the Japan Stroke Society has accredited at least one PSC facility in the secondary medical area and accepts stroke patients on a 24-hour basis. Facilities with 3 or more practical physicians for MT among PSCs will more actively perform MT as PSC cores. Through these measures, the number of cases of MT has increased and uniformity has progressed, but with the aim of improving outcomes by shortening the time from the onset to recanalization, we have started collaboration between hospitals using ICT and trials of stroke bypass using the pre-hospital stroke scale. In clinical studies, 204 patients were enrolled in the SKIP study, a randomized controlled trial of Bridging therapy, which is the usual treatment for patients with IC/M1 occlusion for which intravenous alteplase therapy is indicated, and Direct MT without intravenous alteplase therapy. Finally, the non-inferiority of Direct MT could not be demonstrated in this study. In addition, 203 patients were enrolled in the RESCUE-LIMIT study, a randomized controlled trial of MT and conservative treatment for extensive infarction in ASPECTS3-5, and it was revealed that the MT group had a favorable outcome.
The efficacy of intravenous and endovascular recanalization treatment has been proven through randomized clinical trials and clinical experience. However, there remain several issues that need to be tackled. Ensuring the accessibility of the general population to proven revascularization treatment and high-quality in-hospital stroke care is one of the most urgent directions for stroke physicians. In Korea, three distinct strategies are suggested to integrate emergent medical services and comprehensive stroke centers, providing seamless and continual acute stroke care. Regional characteristics such as advanced stroke care services distribution, geography, and local population influence those three distinct strategies. The organization of regional stroke care services needs to combine all the interests, including local politics, regional administrations, and competing sectors.
Both intravenous tissue plasminogen activator and mechanical thrombectomy are indispensable in hyperacute stroke treatment today. Although the evidence of usefulness and favorable outcome regarding ‘mothership’ approach for mechanical thrombectomy are increasing, that cannot be introduced in everywhere. In a shortage of medical resources, a regional cooperative system for acute stroke treatment is important. In 2016, only 4 actual neuro-interventionalists in 3 stroke centers were available in our prefecture. We decided, until the number of neuro-interventionalists reached up to the satisfactory level, to administer a cooperative medical system using a hotline to receive a request of acute stroke treatment from hospitals throughout the region (Kumamoto EliminAting Regional THrombectomy disparity: K-EARTH) in 2017. The hotline enabled smooth selection of acute care hospital, provision of information regarding emergent care to the client, and rapid transport by car or helicopter. Numbers of patients who received mechanical thrombectomy increased every year after administration of the system. In the meantime, the number of endovascular physicians increased gradually. However, there still remains several issues: patient transportation for long time from outlying regions is difficult due to a lack of attendant physician especially in ‘drip and ship’ approach; helicopters are unavailable in the night and rough weather; a request of acute stroke care itself might be difficult for non-stroke physicians. In summary, cooperative medical system for mechanical thrombectomy K-EARTH using a hotline might be a useful model in regions having a shortage of medical resources. Adaptable system to each medical region and perpetual minor modification is important in acute stroke management.
Symposium 2

SY2-1 Machine learning in classification of CE stroke

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Background
Although chest radiographs have not been utilised well for classifying stroke subtypes, they could provide a plethora of information on cardioembolic stroke. This study aimed to develop a deep convolutional neural network that could diagnose cardioembolic stroke based on chest radiographs.

Methods
Overall, 4,064 chest radiographs of consecutive patients with acute ischaemic stroke were collected from a prospectively maintained stroke registry. Chest radiographs were randomly partitioned into training/validation (n = 3,255) and internal test (n = 809) datasets in an 8:2 ratio. A densely connected convolutional network (ASTRO-X) was trained to diagnose cardioembolic stroke based on chest radiographs. The performance of ASTRO-X was evaluated using the area under the receiver operating characteristic curve. Gradient-weighted class activation mapping was used to evaluate the region of focus of ASTRO-X. External testing was performed with 750 chest radiographs of patients with acute ischaemic stroke from 7 hospitals.

Findings
The areas under the receiver operating characteristic curve of ASTRO-X were 0.86 (95% confidence interval [CI], 0.83–0.89) and 0.82 (95% CI, 0.79–0.85) during the internal and multicentre external testing, respectively. The gradient-weighted class activation map demonstrated that ASTRO-X was focused on the area where the left atrium was located. Compared with cases predicted as non-cardioembolism by ASTRO-X, cases predicted as cardioembolism by ASTRO-X had higher left atrial volume index and lower left ventricular ejection fraction in echocardiography.

Interpretation
ASTRO-X, a deep neural network developed to diagnose cardioembolic stroke based on chest radiographs, demonstrated good classification performance and biological plausibility.
Ischemic stroke is the leading cause of disability and early death, but its genetic determinants remain unknown. Moyamoya disease, a rare cerebrovascular disease endemic in East Asia, is associated with a susceptibility gene named RING finger protein 213 (RNF213) and is characterized by progressive stenosis of the intracranial large arteries. We thus hypothesized that RNF213 plays a more general role in ischemic stroke and examined the association of the p.R4810K variant of the RNF213 gene, the most common risk for moyamoya disease, with ischemic stroke and its subtype. We analyzed case-control data of 47129 individuals of East Asia ancestry (17662 cases and 29430 controls) from three independent Japanese studies of ischemic stroke. For ethnic comparison, we further analyzed case-control data of 1689 individuals of European ancestry. In addition, we performed a meta-analysis of East Asian under a fixed-effects model. A combined meta-analysis of East Asia showed a consistent association of the p.R4810K variant with overall ischemic stroke (OR 1.91, 95% CI 1.55-2.36, P=1.5x10^{-9}) and large-artery atherosclerosis (OR 3.58, 95% CI 2.55-5.03, P=2.0x10^{-13}). We further analyzed 48 early-onset stroke patients with intracranial arterial stenosis and identified the p.R4810K variants in 35% of the patients (OR 25.0, 95% CI 1.4-438, P<0.01). In Caucasians, the p.R4810K variant was scarce and not associated with ischemic stroke risk. The discovery of the strong association of the RNF213 p.R4810K variant with East-Asian ischemic stroke patients with intracranial arterial stenosis has opened new avenues for investigation in the mechanism behind and treatment strategies for intracranial large artery disease. Moreover, we analyzed 277 ischemic stroke patients who underwent endovascular therapy for acute occlusion of the intracranial internal carotid artery or M1 segment of the middle cerebral artery and identified the p.R4810K variants in 3.6% of the patients. Variant carriers had a higher rate of instant re-occlusion (70.0% vs. 5.6%, P<0.001; age-adjusted OR 33.24, 95% CI 6.73–220.48), and early re-occlusion was more frequent in variant carriers compared with non-carriers (60.0% vs 0.4%, P<0.001; age-adjusted OR 198.32, 95% CI 22.75–8503.74). It is necessary to advance further research on the new disease concept "RNF213-related arteriopathy".
The term digital health has its roots in electronic health, which is defined as the use of information and communication technologies to help or support health and health-associated areas. Generally, digital health includes systems, platforms and technologies regarding health, lifestyle, and wellness related purposes. Digital therapeutics (DTx) is a section of digital health defined by the Digital Therapeutics Alliance as “delivering evidence-based therapeutic interventions to patients that are driven by software to treat or prevent various diseases or disorders. DTxs can be used independently or concomitantly with other therapies such as devices or medications to improve or optimize health care”. DTx could overcome limitations associated with classical clinical practice, decrease costs related to attending clinics or hospitals. Moreover, DTx may improve adherence to prescribed medications and healthy behavior. In addition, DTx could also allow continuous monitoring and optimize the time of routine works or treatment behaviors/tasks. For these reasons, even in chronic diseases with disabling characteristics could benefit from DTx. DTx tools usually include screen devices for example videogames, computers, tablets, and smartphones. In this presentation, mainly, review of the implications of DTx in the treatment of neurological deficits for stroke will be demonstrated. The implications of DTx will be discussed in four fields: motor speech disorders, aphasia, visual disturbance, and motor weakness.
Multilineage-differentiating stress enduring (Muse) cells which are endogenous non-tumorigenic stem cells exhibiting pluripotency, collectable as pluripotent surface marker, SSEA-3, from various kinds of sources such as the bone marrow (BM), peripheral blood, and connective tissue. While their proliferative activity is not exponential, their doubling time is ~1.3 day/cell division, and therefore, clinical scale is available in Muse cells. After transplantation, Muse cells recognize and migrate to the injured site through S1P-S1P receptor 2 signaling, and repair the tissue, delivering functional and structural regeneration. Based on these unique properties, the simple strategy; collect Muse cells by SSEA-3, expand them and treat patients by systemic administration, rendering gene introduction and/or induction into purposive cells in cell processing center unnecessary, is available.

We reported that Muse cells not only preferentially integrated into damaged area, but they also spontaneously differentiated into neuronal cells, extended neurites from the cortex into the spinal cord that reformed synapses with host neurons and conducted the reconstruction of pyramidal tract with pyramidal decussation as well as the sensory circuit after middle cerebral artery occlusion in rats. They also repaired neural circuits and improved neural function after subcortical infarction in rats in the subacute phase. Clinical grade Muse cell-based product CL2020 also demonstrated to improve neurological functions after mouse subcortical infarction. CL2020 was intravenously administered at the subacute phase or chronic phase, and the treated animals showed stable functional recovery. After verifying the proof-of-concept, we have conducted a phase II clinical trial for subacute ischemic stroke. In conclusion, Muse cell therapy is promising for the treatment of ischemic stroke. We anticipate the development of cell-based therapies using not only Muse cells but also a variety of other stem cells in the future.
Symposium 3

SY3-1 CADASIL: An Update

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Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is one of the most common single gene disorders of the cerebral small blood vessels caused by mutations in the NOTCH3 gene on chromosome 19q12. Main clinical features included recurrent stroke, migraine, psychiatric symptoms, and progressive cognitive decline. Originally, CADASIL was known to be very rare with an estimated prevalence of 2-4 per 100,000 people. However, recent studies suggest much higher prevalence of pathogenic NOTCH3 variants among general population and the presence of the variants was associated with increased risk of stroke and radiological marker of cerebral SVD. In East Asia, pathogenic NOTCH variants account for 3.5-6.5% of stroke of small vessel origin while only 1.2% of lacunar stroke under 70 years had pathogenic NOTCH variants in the UK. Of the brain small vessel disease markers, the lacunes were independently associated with disability and cognitive dysfunction in patients with CADASIL in cross-sectional studies. In contrast, the white matter hyperintensity lesion load and microbleeds were not associated with cognitive dysfunction after correcting for age. Brain atrophy was also independently associated with age and volume of lacunar lesions but not with white matter hyperintensities or microbleeds in CADASIL. Several promising blood biomarkers have been identified in patients with CADASIL and in a mouse model of CADASIL. Serum neurofilament light chain level was associated with the presence of ischemic or hemorrhagic stroke, neurologic deficit, cognitive dysfunction and overall disability at baseline, and it predicted incident stroke, cognitive decline, disability, or even mortality in patients with CADASIL. However, the level was also elevated in sporadic cerebral SVD and other various neurological disorders and therefore it is not specific for CADASIL. In a mouse model of CADASIL, blood level of Notch3 extracellular domain was significantly decreased in CADASIL while endostatin and high-temperature requirement protein A1 (HTRA1) was elevated compared to controls. Proteomic analysis of human brain arteries disclosed several important proteins whose levels differ significantly between patients with CADASIL and controls. Molecular function or biological process of the proteins included extracellular matrix constituents, cytoskeleton, protein processing and vesicular traffic, and cell adhesion.
Symposium 3

SY3-2  Hemorrhagic small vessel disease markers in Asia

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There are major differences in the epidemiology of ICH, a key clinical phenotype of SVD, by geography or ethnicity; for example, there is a 2-fold higher incidence in Eastern compared to Western countries. Thus, there is major interest in whether the spectrum of SVD pathology differs between different geographic populations and ethnicities. Cerebral microbleeds (CMBs) and spontaneous intracerebral hemorrhage (ICH) are unique among SVD imaging biomarkers because of the well-established association between the topographic distribution of their lesions and pathology of SVD: the lesions in the deep and/or infratentorial (D/I) areas are associated with known markers of hypertensive arteriopathy, whereas those in strictly lobar regions are associated with CAA. Such unique distributional pattern of hemorrhagic small vessel disease markers allowed us to tested the hypothesis that the anatomical distribution of CMBs and spontaneous ICH differs between Eastern and Western populations using individual cohort data.

Regarding CMBs, we conducted a large stroke-free individual participant data (IPD) meta-analysis: In multivariable mixed effects models analyzed with 8,595 stroke-free individuals (mean age, 66.7 years), Eastern populations had higher odds of D/I or mixed CMBs (adjusted OR 2.78, 95%CI 1.77–4.35) compared to Western populations. Eastern populations had a higher number of D/I or mixed CMBs (adjusted prevalence ratio 2.83, 95% CI 1.27–6.31).

Regarding spontaneous ICH, we performed international cross-sectional study included consecutive spontaneous ICH patients admitted to one stroke center in the United Kingdom (Western center origin) and one in Japan (Eastern center origin) during the same period. We classified spontaneous ICH into “CAA-related” or “other” using the Edinburgh CT-based diagnostic criteria. In the multivariable logistic regression model analyzed with 433 patients (median age, 72 years), Eastern center and ethnicity had a lower proportion of CAA-related ICH (OR 0.55, 95%CI 0.31–0.98; OR 0.47, 95%CI 0.25–0.87). We found that the estimated incidence of “other” (non-CAA) ICH (attributed to hypertensive arteriopathy) was 2.5-fold higher in East Asian populations. These findings added novel evidence that there is clear difference in the spectrum of predominant underlying SVD between East and West, suggesting, with potential implications for SVD diagnosis and treatment.
Symposium 3

SY3-3  Prediction of Post-stroke Cognitive Impairment after Acute Ischemic Stroke using Machine Learning Approach

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Background: Post-stroke cognitive impairment (PSCI) may occur in up to 50% of patients with acute ischemic stroke. Thus, the prediction of cognitive outcomes in acute ischemic stroke may be useful in treatment decisions. Machine learning methods are being adopted for use in the prediction, treatment decisions, and prognostication of patients with acute stroke due to their high accuracy. This PSCI cohort study aimed to determine the applicability of the machine learning approach to predict post-stroke cognitive impairment after stroke.

Methods: This was a retrospective study using a prospective PSCI cohort that enrolled patients with acute ischemic stroke. Demographic features, clinical characteristics along with brain image variables formerly known to be associated with PSCI were included in the analysis. The primary outcome was PSCI at 3-6 months, defined as having an adjusted z-score of less than -2.0 standard deviation in at least one of the 4 cognitive domains (memory, executive/frontal, visuospatial, and language) from the Korean version of vascular cognitive impairment harmonization standards neuropsychological protocol. We developed 4 machine learning models (logistic regression, Support Vector Classifier, XGBoost, and Artificial Neural Network) and compared their accuracy in both outcomes.

Results: A total of 1047 patients (mean age 65.7±11.9; male 61.5%) with acute ischemic stroke were included in this study. The area under the curve for the Multilayer perceptron and XGBoost was the highest (0.9432 and 0.9343, respectively) among the 4 models in predicting PSCI according to the VCIHS-NP definition. The most important features for the prediction of PSCI included the presence of cortical infarcts, mesial temporal lobe atrophy, initial stroke severity, previous stroke history, and strategic lesion infarcts.

Conclusions: Our findings indicate that machine learning algorithms, particularly multilayer perceptron and XGBoost models can best predict cognitive outcomes after ischemic stroke.
Symposium 3

SY3-4  Post-stroke epilepsy – Up-to-Date

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With advances in acute stroke treatment, the mortality rate of stroke is dramatically improved. At the same time, the number of stroke survivors has consequently increased due to the aging society. Stroke survivors exhibit a wide range of neurological, physical, and psychological issues. Out of these issues, post-stroke epilepsy (PSE) is a significant clinical issue, occurring in approximately 5%–10% of stroke survivors. Developing PSE is associated with worse clinical outcomes and adversely affects the quality of life. The management of PSE is crucial for stroke survivors. In this session, I will talk about the definition of PSE, risk stratification models, the association with small vessel disease, and the optimal approach for PSE treatments.
Symposium 4

SY4-1  Tenecteplase and thrombolytics under development

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Timely and successful reperfusion is the cornerstone of the acute ischemic stroke treatment. Alteplase is currently the only Food and Drug Administration approved thrombolytic for acute ischemic stroke, and use of intravenous alteplase is the fastest and easiest way to initiate acute stroke reperfusion therapy. Clinical trials with alteplase have consistently shown improvement in neurological and functional outcome of acute ischemic stroke patients. However, the clinical effect of alteplase is still insufficient, and a large portion of ischemic stroke patients with timely use of alteplase did not achieve reperfusion and did not show clinical improvement. Alteplase also had limitations of increased bleeding risk, potential neurotoxicity, and short half-life. Therefore, there is need for the development of more efficient thrombolytics, a clot busting drug for acute ischemic stroke. Tenecteplase is a third-generation multiple point mutant of alteplase. Compared to alteplase, tenecteplase has 15-fold higher greater fibrin specificity and higher plasminogen activator inhibitor-1 resistance. With the longer half-life, tenecteplase can be administered as a single intravenous bolus. Based on the evidence of clinical trials, the single bolus injection of tenecteplase has been approved by the US Food and Drug Administration for the treatment of acute myocardial infarction. Although tenecteplase has not been approved by the FDA as a thrombolytic treatment for acute ischemic stroke, there are a number of clinical trials and researches on the use of tenecteplase in acute cerebral infarction. Accumulated clinical trial data support that tenecteplase is an effective thrombolytic for acute ischemic stroke and may be superior to alteplase. There are ongoing clinical studies to prove the effectiveness and safety of tenecteplase on acute ischemic stroke and to explore appropriate dose and indications.
Secondary stroke prevention in both acute and chronic phases is important. In general, cerebral arterial blood flow rates are high, and aggregation of platelets rather than the coagulation system plays a major role in cerebral thrombus formation in situ. Therefore, antiplatelet agents, sometimes dual application, are chosen for large-vessel atherosclerosis. However, classical studies have also supported the efficacy of warfarin for secondary prevention of stroke in both patients with intracranial and cervical arterial stenosis. One of the main problems observed with the use of warfarin is an increased risk of hemorrhagic complications. Use of the recently developed direct oral anticoagulants (DOACs) entails a low risk of hemorrhagic complications and has contributed to the prevention of deep venous thrombosis (DVT) and venous thromboembolism (VTE), in which the coagulation system plays a pivotal role in slowing the venous flow. In addition, DOACs are recommended for inhibiting thrombus formation in the left atrium in patients with atrial fibrillation (Af). Some studies suggest that DOACs may be useful for preventing recurrent stroke in patients with large-vessel atherosclerosis. For preventing hemorrhagic complications, inhibition of factor Xla appears to be an attractive strategy. Emerging evidence suggests that targeting factor Xla, a key component of the intrinsic pathway, is useful for attenuating thrombosis with little disruption of hemostasis. Patients with congenital factor XI deficiency are at a lower risk of VTE than patients with normal factor Xla levels, and they rarely develop spontaneous bleeding. There are at least four different classes of factor Xla inhibitors that are currently available: 1) antisense oligonucleotides (ASOs), 2) monoclonal antibodies, 3) small molecule drugs, and 4) vaccines. Some recent clinical studies have revealed that they are as safe as low-molecular-weight heparin (LMH) in terms of the risk of hemorrhage, and not inferior to LMH for prevention of VTE in patients who have undergone total knee arthroplasty (TKA). Clinical trials to evaluate the efficacy and safety of small-molecule factor Xla inhibitors for secondary prevention of non-cardioembolic stroke are ongoing. Herein, we report information covering the current status of factor Xla inhibitors for discussing the future directions.
Endovascular thrombectomy (EVT) in addition to intravenous tissue plasminogen activator (IV t-PA) has become the standard of care in acute ischemic stroke with large vessel occlusion. Although both treatments have achieved the advancement of functional independence and mortality rate, the magnitude of outcome advancement has not been proportional to the recanalization rate of the occluded vessels. This discrepancy leads to urgent need for adjunctive therapies such as neuroprotectants to further improve outcomes after recanalization EVT with/or without IV t-PA.

Recently, nerenitide, an eicosapeptide that interferes with post-synaptic density protein 95, gave a light to this need for neuroprotectants in patients with large vessel occlusion who underwent EVT. The use of narenitide was associated with good functional outcome and reduction in infarction volume in the patients who underwent EVT without IV t-PA. In addition, the phase III ongoing trial using nelonemdaz, a multi-target neuroprotectant preventing both the N-methyl-D-aspartate receptor, a Ca\textsuperscript{2+}-permeable glutamate receptor, and free radicals, are conducted in the patients with large vessel occlusion who underwent reperfusion therapy based on promising result of phase II trial and other pharmacotherapy using magnesium and verapamil are ongoing.

Previous many trials related to neuroprotectants in ischemic stroke were failed to show the efficacy. However, current several trials showed the possibility of improving the patients’ outcome without serious adverse effect in ischemic stroke patients. Thus, neuroprotectants as adjunctive therapy after recanalization therapy in ischemic stroke seems to be feasible in near future.
Symposium 4

SY4-4  Efficacy and safety of prasugrel versus clopidogrel in thrombotic stroke patients with risk factors for ischemic stroke recurrence

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Antiplatelet agents such as aspirin, cilostazol, and clopidogrel are used for the prevention of recurrence of non-cardioembolic stroke. Because the risk of stroke recurrence is still high, several new antiplatelets have been developed and are under development. One of issues to be solved is genetic polymorphisms in cytochrome P450 (CYP) 2C19 that contributes to a poor response to clopidogrel, which raises concerns about clopidogrel monotherapy in Asian people, who are more likely than white people to be CYP2C19 poor metabolizers. In this session, I will introduce characteristics of prasugrel and three phase 3 trials of prasugrel conducted in Japanese patients with ischemic cerebrovascular disease: PRASTRO-I, PRASTRO-II, and PRASTRO-III. Prasugrel, a relatively new P2Y12 receptor antagonist, has been shown to inhibit platelet aggregation more rapidly and consistently, and to a greater extent, than clopidogrel independently of CYP2C19 genetic polymorphisms. Three PRASTRO trials had the same primary efficacy endpoint, a composite incidence of stroke, myocardial infarction, and death from other vascular causes. Although PRASTRO-I did not prove the non-inferiority of prasugrel to clopidogrel, a subgroup analysis revealed a 20% risk reduction in patients with large-artery atherosclerosis or small-artery occlusion treated with prasugrel versus clopidogrel. In PRASTRO-II, the efficacy and safety of prasugrel and clopidogrel were similar in elderly and/or low body weight Japanese patients. PRASTRO-III, which included patients ≥50 years of age who had thrombotic stroke and were at risk of ischemic stroke, showed the possible efficacy of prasugrel. Based on these findings, prasugrel was approved in Japan for the indication of recurrence prevention after ischemic cerebrovascular disease (associated with large-artery atherosclerosis or small-artery occlusion) in patients with a high stroke risk.
In the case of successful recanalization by intraarterial thrombectomy (IAT), a similar guideline of intravenous tissue plasminogen activator (IV tPA) is adopted. However, recanalization rates with IAT are much higher compared with IV tPA alone, and it remains unclear if the same BP targets can be applied. High blood pressure (BP) may result in reperfusion injury or intracerebral hemorrhage. On the other hand, too low BP can worsen cerebral ischemia. Outcome in Patients Treated with Intraarterial thrombectomy - optiMAL Blood Pressure control (OPTIMAL-BP) trial (ClinicalTrials.gov, NCT04205305) is a multicenter, prospective, randomized, open-label trial with blinded end-point assessment (PROBE) design. After successful recanalization, patients will be randomly assigned to a strategy of intensive BP lowering (systolic BP < 140 mm Hg) group or conventional BP control (systolic BP 140 -180 mm Hg) group. Prespecified two primary effectiveness outcomes will be assessed at 3 months with intention-to-treat analysis. One is the conventional dichotomized analysis of modified Rankin scale scores (mRS) at 3 months [mRS 0-2 (functional independence) vs. 3-6 (major disability or deaths)]. The other is a shift analysis of mRS. A shift in functioning measures according to the full range of scores on the mRS will be analyzed. The primary safety outcome will be the occurrence of symptomatic intracerebral hemorrhage and death related to the index stroke within 3 months. We will enroll the patients who achieved successful recanalization (thrombolysis in cerebral infarction [TICI] score ≥2b) and elevated systolic BP level, defined as ≥140 mmHg within 2 h after successful recanalization. Following randomization, BP measurements will be recorded every 15 min for the first 1 h, hourly until 24 h. To achieve and maintain BP targets, local BP treatment protocols with intravenous BP lowering drugs will be used. OPTIMAL-BP study will enroll 668 patients and be conducted until August 2024. The study will shed light on the question of optimal BP control within 24 h after successful recanalization by IAT.
Introduction: Effectiveness of endovascular therapy for acute cerebral large vessel occlusion was approved in patients with the Alberta Stroke Program Early CT Score (ASPECTS) ≥ 6. However, its effectiveness for patients with large ischemic core defined as ASPECTS of 3-5 was uncertain.

Methods: RESCUE-Japan LIMIT was a multicenter, randomized, open-label, parallel-group clinical trial to attest the superiority of endovascular therapy compared to medical therapy only in patients with acute cerebral large vessel occlusion with large ischemic core defined as ASPECTS of 3-5. Patients were randomly assigned to receive endovascular therapy or medical therapy alone. The primary outcome was a moderate functional outcome defined as modified Rankin Scale (mRS) score ≤ 3 at 90 days. The secondary outcomes were one scale shift of mRS score, good functional outcome (mRS ≤ 2), excellent functional outcome (mRS ≤ 1), and mortality at 90 days as well as early improvement of neurological findings at 48 hours.

Results: We enrolled 203 patients (101 in endovascular therapy; 102 in medical therapy without endovascular therapy) from November 2018 through September 2021, and complete the follow-up on December 2021. A total of 203 patients underwent randomization; 101 patients were assigned to the endovascular-therapy group and 102 to the medical-care group. Approximately 27% of patients in each group received alteplase. The percentage of patients with a modified Rankin scale score of 0 to 3 at 90 days was 31.0% in the endovascular therapy group and 12.7% in the medical-care group (relative risk, 2.43; 95% confidence interval [CI], 1.35 to 4.37; P = 0.002). The ordinal shift across the range of modified Rankin scale scores generally favored endovascular therapy. An improvement of at least 8 points on the NIHSS score at 48 hours was observed in 31.0% of the patients in the endovascular-therapy group and 8.8% of those in the medical-care group (relative risk, 3.51; 95% CI, 1.76 to 7.00), and any intracranial hemorrhage occurred in 58.0% and 31.4%, respectively (P<0.001).

Conclusions: In a trial conducted in Japan, patients with large cerebral infarctions had better functional outcomes with endovascular therapy than with medical care alone but had more intracranial hemorrhages.
### Symposium 5

**SY5-3  DURATION (Dual antiplatelet Use for extended period taRgeted to AcuTe Ischemic stroke with presumed atherosclerotic OrigiN) Trial: Rationale and Designs**

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**Rationale:** Optimal duration of dual antiplatelet therapy with clopidogrel-aspirin (DAPT) in stroke of large artery atherosclerotic (LAA) subtype remains a point of great controversy.

**Aim and/or hypothesis:** To determine whether the 1-year risk of recurrent vascular events could be reduced with longer duration DAPT in LAA stroke subtype.

**Sample size estimates:** A total of 4,806 participants will be recruited in order to be able to detect statistically significant between-group difference of a relative risk reduction of 22% with 80% power at a two-sided alpha of 0.05, including 10% lost to follow-up.

**Methods and design:** This trial is a registry-based, multicenter, prospective, randomized, open-label, blinded endpoint study designed to evaluate the efficacy and safety of a 12-months duration of DAPT compared to a 3-months duration of DAPT in ischemic stroke of LAA subtype. Patients are randomized to either long-duration of dual therapy with clopidogrel-aspirin (12 months group) or 3-months dual therapy with clopidogrel-aspirin, followed with monotherapy (either aspirin or clopidogrel) for remaining 9 months (3 months group).

**Study outcome:** Primary efficacy outcome of the study is a composite of stroke (either ischemic or hemorrhagic), myocardial infarction and all-cause mortality for 1-year after index stroke. Secondary efficacy outcomes are 1) stroke (either ischemic or hemorrhagic), 2) ischemic stroke or transient ischemic attack, 3) hemorrhagic stroke, and 4) all-cause mortality. Primary safety outcome is major bleeding defined as the Bleeding Academic Research Consortium criteria.

**Discussion:** This study will provide valuable clarification of the appropriate duration of dual therapy with clopidogrel-aspirin for LAA subtypes stroke patients.
Symposium 5

SY5-4  Stoke secondary prevention with and without catheter ablation in patients with recent ischemic stroke and non-valvular atrial fibrillation: The STABLED study

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\textbf{Background:} Catheter ablation (CA) has been reported to reduce risk of in patients with nonvalvular atrial fibrillation (NVAF) in retrospective studies. However, the risks and benefits of CA have not been well elucidated in patients with NVAF and who have suffered a recent ischemic stroke in prospective randomized trials. Thus, the aim of the STABLED clinical trial is to investigate the efficacy and safety of CA with anticoagulant therapy using edoxaban in patients with NVAF and a history of recent ischemic stroke.

\textbf{Methods and design:} The STABLED trial is a multicenter, prospective, randomized, open-label, standard medication-controlled study in Japan. The target patient number is 250, comprising 125 patients receiving standard medication and 125 receiving CA. For patients allocated to the CA group, ablation is to be performed between 1 to 6 months from the onset of index stroke. The observation period will be 3 years from the day of random allocation of the final patient to any of the groups. The primary outcome measure is the composite of recurrence of ischemic stroke, systemic embolism, all-cause death, and hospitalization for heart failure.

\textbf{Conclusion:} This study will investigate the effectiveness and safety of CA and basic anticoagulation treatment with edoxaban for patients with NVAF who have suffered a recent ischemic stroke. The aim is to determine the best evidence for an optimal treatment strategy for patients with NVAF and recent stroke. Now we already enrolled 253 patients as target number of cases and have been followed the patients. The study will be end in April 2024.
**Symposium 6**

**SY6-1  Health policy to stroke in Korea**

Jihoon Kang  
Seoul National University, Korea

**Background:** The health care system of Korea has been developed under a unique single government-operated national health insurance service (NHIS) program since 1963. Based on that system, mainly privately owned hospitals decided to participate in stroke care and provided various treatments in their capacity. At the prehospital step, the nation operates a single emergency medical transport system and is currently implemented to triage stroke suspicious to a nearby stroke care hospital.

**Status and renovation:** The Health insurance review and assessment (HIRA) checked the quality indicators of acute stroke care hospitals. It reported a higher performance in the early administration of tPA compared to those of the US and Taiwan (94.6%, 90.3%, and 8.8%, respectively); however, it demarcated the wide hospital disparities, especially in defect-free stroke care (all-or-none) were reported (hospital mean = 50.7%; SD = 21.7%). At a regional level, they presented the extortionate gap of three-fold for IVT and more than twice for EVT.

The national data from the NHIS and HIRA presented a spontaneous formation of the stroke network; in short, patients with ischemic stroke initially visited 1009 hospitals, of which about 20% transferred to be merged into 246 stroke care hospitals within a day without pre-defined hospital transfer rules.

In line with the global trend, it tried to establish the hub-and-spoke system for jointly providing the utmost treatment in consideration of regional-specific circumstances. A pilot project to set up a natural practice-friendly linkage system linked a primary stroke hospital to the comprehensive center to make a direct hotline system between physicians and a web-based imaging transmission service. It reported the effective tPA in the first hospital and subsequent advanced treatment via a linkage system.

**Conclusion:** An accurate estimation of the current situation and appropriate political plans would be essential for developing privately owned hospitals and the government's insurance system.
Cerebrovascular disease, including stroke, and cardiovascular disease are the leading causes of death in Japan, which together account for 23.2% of the total number of deaths in 2018. The major causes of the need for long-term care in Japan are also cerebrovascular disease (16.1%) and cardiovascular disease (4.5%), which together account for more than one-fifth of the total. The Stroke/Cerebrovascular and Cardiovascular Disease Control Act, of Japanese national law, was promulgated by a legislative act on December 14, 2018, and enacted on December 1, 2019. On the basis of the Stroke/Cerebrovascular and Cardiovascular Disease Control Act, the Ministry of Health, Labour and Welfare, Japan, published the Japanese National Plan for Promotion of Measures Against Cerebrovascular and Cardiovascular Disease (Japanese National Plan) on October 27, 2020. The 2 main goals of the plan are to extend healthy life expectancy by 3 years by 2040 compared with 2016 and to decrease age-adjusted mortality of cerebrovascular and cardiovascular disease. To promote a wide range of cerebrovascular and cardiovascular disease measures, the plan includes 3 major measures: spreading awareness of prevention measures and accurate information on cerebrovascular and cardiovascular disease; enhancing service provision systems related to health, medical care, and welfare services; and promoting research on cerebrovascular and cardiovascular disease. Furthermore, on the basis of the plan, each prefecture prepares a cerebrovascular and cardiovascular disease countermeasure promotion plan to progress cerebrovascular and cardiovascular disease measures according to circumstances in each region.

### National Plan for Promotion of Measures Against Cerebrovascular and Cardiovascular Disease

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Prevention (Primary, Secondary, and Tertiary)</th>
<th>Acute phase</th>
<th>Recovery—Chronic phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Measures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>[Base]</strong></td>
<td>Establishing a system for collecting and providing medical information on CVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Spreading awareness of prevention measures and accurate information on CVD</td>
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<td>2.</td>
<td>Enhancing service provision systems related to health, medical care, and welfare services</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1)</td>
<td>Promoting health checkups to prevent CVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2)</td>
<td>Improving emergency transportation systems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(3)</td>
<td>Securing emergency medical care and establishing medical care provision systems for CVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4)</td>
<td>Providing measures against CVD based on social cooperation and patient support</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(5)</td>
<td>Developing a system to provide medical care and rehabilitation for CVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(6)</td>
<td>Providing appropriate information and consultation support for CVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(7)</td>
<td>Providing palliative care for CVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(8)</td>
<td>Supporting patients with after-effects of CVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(9)</td>
<td>Providing support for balancing treatment and work</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(10)</td>
<td>Providing measures for CVD that need consideration from childhood and young adulthood onward</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3. Promoting research on CVD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Research and development contributing to the elucidation of the pathogenesis of CVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Methods for prevention, diagnosis, treatment, and rehabilitation, etc.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Goal</strong></td>
<td>To extend healthy life expectancy for 3 years by 2040 compared with 2016</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>To decrease age-adjusted mortality of cerebrovascular and cardiovascular disease</td>
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</tbody>
</table>
Stroke is a leading cause of death and disability worldwide, although considerable portion of this fatal disease can be preventable by effective vascular risk factor control and life style modification. Moreover, recent advancement and implementation of the reperfusion therapy and intensive medical management with stroke unit decreases mortality rate following acute stroke. However, there are a lot of unsolved problems in stroke management continuum, such as optimization of recanalization therapy, stroke etiology evaluation, recurrence prevention, recovery promotion, which requires research effort of experts from diverse fields. The management principle for hemorrhagic stroke is still limited to vascular risk factor control and the prevention of acute medical complication. Several miscellaneous stroke etiologies including moyamoya disease or cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy are more frequently found among Asian than Western population, thus these disease entities have not drawn attention of investigators outside of Asia. Accordingly, adequate academic research support is a paramount strategy to facilitate multidisciplinary team works which can bring an innovation in stroke management. I will introduce and discuss about the various types of academic support for stroke research in Korea.
Compared to the oncology and cardiovascular fields, research funding for clinical study in the stroke field is low worldwide. In Japan, the 2015 amendment to the Medical Care Act established core clinical research hospitals. To date, 14 hospitals have been certified and research infrastructure has been developed in these hospitals. They are either university hospitals or cancer centers, however, most of which are not very active institutes for acute stroke care. In 2015, the NeCST (Network for Clinical Stroke Trials) has been established for multicenter clinical studies, based on the institutes which experienced the international clinical trial named the ATACH II. Several clinical studies, including international trials like FASTEST, have been conducted using the NeCST. In the NeCST, The NCVC play a role as the coordination center and data management center, and Iwate Medical University as the central imaging center. As the current clinical research regulations in Japan are very complex, the NeCST informs regulatory knowledge and disseminates a more compliant approach to regulations to participating institutes.
The World Stroke Organization (WSO) Brain & Heart Task Force developed The Brain & hEart globAl iniTiative (BEAT), a pilot feasibility program aiming at establishing clinical collaborations between cardiologists and stroke physicians who work at large healthcare facilities. The WSO BEAT pilot project focused on atrial fibrillation (AF) and patent foramen ovale (PFO) detection and management, highly prevalent cardioembolic causes of ischemic stroke and transient ischemic attack (TIA). The program also focused on the stroke-heart syndrome, given the high incidence of cardiovascular complications observed after stroke.

The pilot feasibility WSO BEAT program included nine sites from eight countries, including Brazil, China, Egypt, Germany, Japan, Mexico, Romania, and the USA. Of the 10 sites, nine belonged to the public sector. The primary objective of the pilot WSO BEAT program was to assess its feasibility by achieving a composite feasibility outcome: (1) developing site-specific clinical pathways for the diagnosis and management of AF, PFO, and the stroke heart syndrome; (2) establishing regular Neurocardiology rounds (e.g., monthly, bimonthly, etc.); and (3) incorporating a cardiologist to the stroke team.

Overall, the WSO BEAT program successfully achieved the pre-specified goals at most sites. Regarding the three primary program objectives, 9/10 (90%) of the sites were able to design or update the proposed clinical care pathways, establish Neurocardiology rounds, and designate a dedicated cardiologist for the stroke team, respectively.

The WSO BEAT pilot program showed that developing Neurocardiology collaborations is feasible. These results should encourage future large-scale initiatives to test its scalability. Ideally, a larger-scale program should focus on identified needs (e.g., poor access to diagnostic technologies and therapeutic procedures) and measure the impact of establishing strong Neurocardiology collaborations on clinical outcomes.
Although brain-heart relationship is not a regional issue in cerebrovascular diseases, valuable researches came from Korea recently. There are briefly two issues in brain-heart relationship in bidirectional way. In the classical aspect, heart rhythm and structural changes affect brain vessels and functions via their pumping activities. Also, the damages of brain from cerebrovascular disease could induce heart problems. According to variable invasive or non-invasive devices monitoring cardiac rhythms, new insight of brain-heart interaction was shown from Korea researchers. They retrospectively selected consecutive patients with an insertable cardiac monitor (ICM) implanted for atrial fibrillation (AF) detection following embolic stroke of undetermined source (ESUS). The primary endpoint was defined as any AF episode lasting for longer than 5 min. The atrial ectopic burden (AEB) was calculated as the percentage of the number of conducted QRS from atrial ectopy on Holter monitoring. AF was detected in a significant proportion of ESUS patients during a 6.6-month follow-up. The LAD and AEB are good predictors of AF and might be useful for AF risk stratification in ESUS patients. Moreover, the second issue related to the direction from brain to heart can be introduced from other Korea researchers. They investigated clinical and radiological characteristics of ischemic stroke patients with Takotsubo-like myocardial dysfunction. From multicenter stroke registry database, ischemic stroke patients who underwent transthoracic echocardiography were found. Among these, patients were classified if they had specific ventricular regional wall motion abnormalities discording with coronary artery distribution, such as apical (typical pattern) or nonapical ballooning (atypical pattern), considered as echocardiographic findings of Takotsubo cardiomyopathy. They showed that Stroke patients with Takotsubo-like myocardial dysfunction may differ from those without in clinical outcomes, laboratory findings, and radiological features. Other than these milestones, Korean researchers is ongoing lots of efforts to study brain-heart interaction.
The importance of Brain-heart team is emphasized based on the recent remarkable progress in device therapy, such as left atrial appendage (LAA) closure and patent foramen ovale (PFO) closure systems. At the National Cerebral and Cardiovascular Center, the departments of stroke and cardiology has been cooperated to the care involving Brain-heart team, including LAA closure, PFO closure, catheter ablation, surgical LAA closure, syncope examination/treatment, and loop recorder implantation.

For percutaneous PFO closure, we have been certified as the CoE (Center of Excellence: a organization that integrates human resources and hardware) for this treatment, of which there are only about 10 facilities in the world. The World Stroke Organization (WSO) launched the WSO-Brain & hEart globAl iniTiative (WSO-BEAT) project to enlighten this team medical treatment. Our center is also certified as one of the eight model facilities in the world and working to raise awareness of this treatment. Regarding the LAA closure, division of arrhythmia in our center committed special efforts to the clinical trials for the approval of this treatment. The division of cardiac surgery also performs left atrial appendage closure by surgery.

On the other hand, the number of facilities that can perform the above device treatment is limited in Japan; 81 facilities for LAA closure system and 87 facilities for PFO closure. In comparison with in United States, the percentage of cases treated with these devices remains low in Japan. Inter-institutional collaboration seems to be necessary for the popularization of the device treatment to patients who need it.
Since the start of the COVID-19 outbreak in end-2019, the number of cases is rising, although the new case rate has been recently falling. An international study showed ischaemic stroke (IS) admissions decreased by 15.1%, intracerebral haemorrhage (ICH) by 11.5%, with 12.7% decrease in mechanical thrombectomy (MT) procedures. A diagnosis of any stroke was present in 1.45% while 3.9% of overall stroke admissions were diagnosed with COVID-19. The pooled incidence of acute IS in COVID-19 patients was 1.2%, mean age 63.4yr, mean duration of AIS from COVID-19 symptoms onset 10dy, mean NIHSS score 19, with large vessel thrombosis/embolism/stenosis 62.1%, multiple vascular territory 26.2%, small vessel pattern 8.7%; 38.0% died. SARS-CoV-2 probably leads to IS by causing a hypercoagulable state, vasculitis, cardiomyopathy, and ICH by virus damage to intracranial arteries causing vessel wall rupture, cytokine storm. A recent stroke care review (Venketasubramanian N, et al. Stroke Care during the COVID-19 Pandemic: International Expert Panel Review. Cerebrovasc Dis. 2021;50(3):245-261) stressed that all patients in the pre-hospital setting should be treated as potential COVID-19 cases until the results of subsequent COVID-19 screening in the hospital are negative; all EMS staff must wear PPE; EMS to pre-notify the target hospital about COVID-19/high-suspect COVID-19 (hsCOVID-19) status, or even send them to designated centres. In the ED, all patients should be screened for COVID-19, with a separate channel/area/scan machine for positive cases; minimise staff, use tele-stroke, minimise aerosol-producing procedures, image at end of day if non-urgent. Throughout the hospital stay, to minimise staff, with all wearing PPE, strict infection control procedures. Evidence-based treatments such as intravenous thrombolysis, MT, prescription of anti-thrombotics should continue. Neurocritical care should be provided for patients who may benefit; aerosol-generating procedures on COVID-19 ICU patients should be performed in a negative pressure room. Non-ICU requiring COVID-19 patients should be nursed in isolation. At least 45mins/dy of each relevant stroke rehabilitation therapy, minimum of 5 dy/wk, tele-rehabilitation encouraged, to facilitate family visits, video-calls, phone calls. Post-discharge clinic visits minimized; use tele-consultation, tele-rehabilitation, home delivery of medications. Clinicians should use the best available evidence to guide them in the management of their patients.
Covid-19 infection and vaccination are still ongoing. The Covid-19 pandemic era had a lot of influence on the treatment of stroke patients in Korea. COVID-19 appears to have affected the stroke chain of survival by hindering entry into EDs with stroke centers, the gateway for acute stroke patients. A retrospective observational study was done in Busan to identify a significant decrease in the number of patients transferred to an ED with a comprehensive stroke center and an increase in time taken to the emergency room (EMS processing time) by about 4 minutes in the COVID-19 period. The total number of patients using EMS for acute stroke symptoms decreased by 8.2% during the COVID-19 period. According to a retrospective study conducted using the Korean Stroke Registry database, the number of acute stroke hospitalizations decreased, and the hospitalization period was longer in the COVID-19 pandemic era compared to pre-COVID-19. According to a comparative cross-sectional study conducted in 25 safety centers in Seoul, there was no significant difference between baseline characteristics and clinical outcomes of patients with acute stroke before and after the COVID-19 outbreak. However, another case series report showed a tendency to develop a lot of multiple embolic infarctions as a major mechanism for stroke that occurred in the early phase of COVID-19. COVID-19 outbreak immediately affected the management process. The process of emergency medical services has been modified to ensure the safety of healthcare professionals as well as patients in Korea. In addition, we found a significant increase in door-to-imaging time in the suspected COVID-19 (+) group, and the COVID-19 protection protocol in patients suspected of COVID-19 was also improved. There are no large-scale studies on the risk of COVID-19 and stroke in Korean data. Research is underway to analyze the risk of COVID-19 vaccination and stroke through big data analysis, and when the risk for ischemic stroke and subarachnoid hemorrhage was applied for 28 days, there was no significant relationship between vaccination and ischemic stroke and subarachnoid hemorrhage. In the case of intracerebral hemorrhage, the risk after COVID-19 vaccination was decreased.
Joint symposium by APSO-KSS-JSS

JSY2-3  Covid-19 and stroke in Japan

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Background and Purpose: The purpose of this report is to investigate the impact of the COVID-19 pandemic on the stroke center activity relative to those before the pandemic in Japan.

Methods: Japan Stroke Society (JSS) and MHLW stroke research group conducted a national surveillance of hospitalization volumes for acute ischemic stroke, intracranial cerebral hemorrhage, and subarachnoid hemorrhage in JSS certified PSCs. Number of acute stroke patients was defined as sum of three stroke subtype admitted within 7 days after the onset. Monthly acute stroke volumes were compared between 2019 and 2020 or 2021, among COVID 19 waves, and regional infectious rates.

Results: The stroke volume data was completed in 530 PSCs. The annual acute stroke volume was declined 2.5% from 179,893 in 2019 to 174,385 in 2020. Number of acute stroke patients was declined during COVID 19 expanding periods (1st wave, Mar-May; 2nd wave Jul-Aug; 3rd wave Nov-Dec), whereas it was increased in the other months. The mean decline rate of stroke volumes from 2019 to 2020 was greater in 125 PSCs located in prefectures with high estimated COVID 19 infected rate (more than 2,300 per million people) than in 405 PSCs of the other regions (-4.6±15.4% vs -0.1±20.0%, P=0.008), especially during COVID 19 expanding periods (-8.2±17.9% vs -3.1±21.3%, P=0.009). The inverse correlation continues that as the number of COVID-19 increases, the number of admitted stroke patients decreases in 2021.

Conclusions: Acute stroke volumes was declined in 2020 or 2021 from 2019 in Japanese PSCs, especially during COVID 19 expanding periods and in highly infected regions. The overwhelmed health care system and infection control practices may be associated with decline of number of acute stroke patients during COVID 19 pandemic.
The Japan Stroke Society Guideline 2021 for the Treatment of Stroke (GL2021) was developed and revised adding new knowledge in 2-year intervals by the Guideline Committee of the Japan Stroke Society from the 2015 version (2017 update version and 2019 update version). Although GL 2021 comprises 300 pages in Japanese and includes the broad scope from acute treatment to rehabilitation, the English version, recommendations of each topic are extracted, has been published (Miyamoto S et al. Int J Stroke 2022). In developing GL 2021, we decided to partially incorporate the Guide to the Preparation of Minds Clinical Practice Guideline 2017. This means that in the Guideline Committee, there was no distinction between those who reviewed the literature and those who wrote the recommendations. Moreover, the clinical question format was partially introduced, with five grades of recommendation and three levels of evidence (LOE).

In GL 2021, a direct oral anticoagulant (DOAC) is recommended both for primary prevention of cardioembolic stroke or prevention of stroke recurrence due to nonvalvular atrial fibrillation. Moreover, in accordance with the guidelines of the Japanese Circulation Society and the Japanese Heart Rhythm Society, the target value of PT-INR for warfarin therapy were separately set according to CHADS2 score, other risk factors, and age. DOAC is not recommended for patients with cryptogenic stroke or embolic stroke of unknown cause. Initiation of DOAC during acute phase in patients with ischemic stroke due to NVAF considering the risk of hemorrhagic infarction is also referred. Not only dual antiplatelet therapy (DAPT) for mild non-cardioembolic ischemic stroke or high-risk TIA in the acute phase but also DAPT including cilostazol was referred as secondary prevention in the chronic phase of ischemic stroke. In addition, the following topics were also discussed: the optimal target blood pressure levels in the chronic phase, or percutaneous patent foramen ovale closure for cryptogenic stroke.

In 2023 update version, the new topics to date including mechanical thrombectomy (MT) for patients with low ASPECTS, or skipping intravenous thrombolysis before MT might be referred. Recently, prasugrel for prevention of stroke recurrence has been approved in Japan.
A decade has passed since we got the first DOAC for stroke prevention in patients with non-valvular atrial fibrillation. For clinicians, DOACs are no longer “newcomers” but one of the very popular and routine-prescribing drugs.

In the warfarin era, bleeding complication, especially intracerebral hemorrhage was the most serious event among both Japanese and Korean patients. So that we often reduced warfarin intensity to avoid bleeding in the clinical setting.

Unfortunately, this custom is still popular even in the DOAC years. Recently, the off-label low dose of Xa inhibitors is nearly half in both countries. It is well known that the most advantage of DOACs besides warfarin is the surprisingly lower incidence of hemorrhagic stroke. The efficacy is almost the same between the two anticoagulants. It means that we should consider efficacy rather than safety as the priority of DOAC administration. In other words, we do not need to hesitate to administrate the full dose of DOACs according to our newest guidelines.

In this session, we together will reconfirm the initial evidence of DOACs from the large global clinical trials once again and try to discuss the real benefit of these drugs, especially apixaban, for patients with atrial fibrillation.
Sponsored seminar 2

SS2  Management and secondary prevention in acute ischemic stroke patients with non-valvular atrial fibrillation: focus on ongoing clinical issues

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About one-third of ischemic stroke is cardioembolic, mainly related to non-valvular atrial fibrillation (NVAF). The mainstream secondary prevention is anticoagulation with direct oral anticoagulant (DOAC) or warfarin. Recently, DOAC is two-three folds more frequently used than warfarin because DOAC has comparable efficacy and significantly more safety profiles than warfarin. There are several ongoing clinical issues which need to be improved.

First, patients taking anticoagulants may have a high risk of hemorrhagic complications following intravenous thrombolysis. Thrombolysis with alteplase at 0.6mg/kg was safely performed in patients taking DOAC following the Japanese guidelines (Okada T, et al. J Am Heart Assoc 2022, in press). Second, evaluation and management of intracardiac thrombus are not standardized in acute cardioembolic stroke because the clinical significance of intracardiac thrombi in patients with NVAF-associated stroke has not been confirmed. Clinical data from Korean and Japanese stroke centers showed that intracardiac thrombi were associated with a risk of recurrent ischemic stroke, and transesophageal echocardiography could provide accurate detection and risk stratification of intracardiac thrombi than transthoracic echocardiography in NVAF-associated stroke (Tanaka K, et al. J Am Heart Assoc 2021;10:e022242).

Third, though randomized clinical trials that tested DOAC did not include acute ischemic stroke patients, observational studies indicated that early initiation of DOAC might be safe and effective (Mizoguchi T, et al. Stroke 2020;51:883-891; Kimura S, et al. Stroke 2022;53:1540-1549.). Ongoing clinical trials to test the early initiation will be finalized in the coming years. Fourth, in patients having a recent acute ischemic stroke, cerebral microbleeds (MBs) are associated with a greater relative hazard for subsequent hemorrhagic stroke than for ischemic stroke, but the absolute risk of ischemic stroke is higher than that of hemorrhagic stroke (Wilson D, et al. Lancet Neurology 2019;18:653-65). The indication of anticoagulation might be under-debate in patients with MBs. Finally, NVAF-associated ischemic stroke patients with prior anticoagulation have a higher risk for recurrent stroke (Tanaka K, et al. Stroke 2020;51:1150-1157). The treatment strategy, perhaps including left atrial appendage occlusion, needs further investigation in those with a high risk of recurrent stroke.
Atrial fibrillation (AF) is a common cardiac arrhythmia that is associated with an increased risk of ischemic stroke, heart failure, and all-cause death. Atrial fibrillation (AF)-related strokes are more severe than other subtypes of stroke. AF detection is crucial for secondary prevention in patients with cryptogenic stroke. Prolonged cardiac rhythm monitoring using implantable loop recorders (ILRs) is useful for detecting underlying AF episodes in patients with cryptogenic stroke. A recent prospective data showed that the higher AF detection by ILRs resulted in the anticoagulation initiation and lower stroke recurrence than conventional cardiac monitoring. The PER DIEM randomized clinical trial showed the 15.3% of AF detection by ILRs in patients with any types of ischemic stroke within 12 months, demonstrating that stroke patients are at high risk of AF. In our hospital, 33% of patients with embolic stroke of undetermined source on admission were finally diagnosed as cryptogenic stroke after the work-up of embolic sources and can be candidates of ILRs implantation. Both the work-up of embolic sources and long-term cardiac monitoring using ILRs have been performed by stroke physicians. In total, ILRs was implanted in 152 patients and AF was detected in 40 patients (26%). The median days between implantation and AF detection was 90 days (interquartile range [IQR], 23–367 days). Patients with AF detected by ILRs had larger left atrial volume index, higher level of BNP and more frequent premature atrial complex. These findings were consistent with previous studies that suggest the importance of cardiac-related indicators for a higher probability of AF detection. P-wave indices and left ventricular dysfunction may also be promising makers that are associated with AF detection by ILRs. ILRs may be useful for AF screening before patent foramen ovale closure especially in elderly patients. ILRs can measure the AF burden, which may help to estimate the frequency of AF. Stroke physicians should intensively search for covert AF in stroke patients and contribute to preventing atrial remodeling with multidisciplinary approach.
The Patent foramen ovale (PFO) has been regarded as a potential cause of ischemic stroke. Many epidemiological or clinical evidence has supported the causal association between PFO and the risk of stroke, especially in stroke patients at a young age, still, there are many unsolved questions for the management of PFO-associated stroke. With the tremendous efforts of the researchers, evidence for the medical and surgical/interventional management of PFO has been accumulated. The current guidelines state that there is no difference in stroke prevention effect between antiplatelet agents and oral anticoagulants. Surgical or interventional PFO closure is recommended in patients with PFO-associated stroke without evidence of other etiology in recent clinical practice guidelines. However, still, many questions are left in the unsolved state for the management of PFO-associated stroke. The clinically relevant definition of the high-risk PFO, age-related decision-making for PFO closure, and the duration or the withdrawal criteria of antithrombotics especially in young stroke patients with PFO. Here, we will discuss the direction of PFO-associated stroke management with an emphasis on the clinical evidence. And the introduction of the nationwide clinical study about PFO-associated stroke will be provided.
Sponsored seminar 4

SS4-2  Brain-Heart approach for Patent Foramen Ovale-associated stroke in Japan and key practices at NCVC.

Masayuki Shiozawa
National Cerebral and Cardiovascular Center, Japan

National Cerebral and Cardiovascular Center (NCVC) is the second oldest national center in Japan with specialized cerebrovascular and cardiovascular facilities. This session is an introduction to guideline-based practice for closure of Patent Foramen Ovale (PFO) -associated stroke and the NCVC brain-heart team approach.
SS5-1  Striking out for tailored mechanical thrombectomy in the era of total stroke solutions

Kanta Tanaka
Division of Stroke Care Unit, National Cerebral and Cardiovascular Center, Suita, Japan

Mechanical thrombectomy for acute stroke is currently performed using either stent retriever, contact aspiration, or a combination of both techniques, and the choice among the three techniques may now depend more upon physician or institutional technical preferences and device availability than on patient factors; however, each thrombectomy technique has different physical properties, so the situations in which one technique stands out among the others are likely to vary depending on vessel tortuosity and the composition of target thrombi. Regarding thrombus composition, thrombi rich in fibrin or platelets have high stiffness and are likely to be difficult to be fully integrated with stent retrievers. Although it is not always easy to clinically determine the presence of such thrombectomy-resistant thrombi, residual thrombi after device passes are considered fibrin-rich. The Trevo NXT stent retriever can adjust its own radial force using the Push & Fluff technique, allowing it to be used according to the assumed clot architecture. The increased platelet content is more strongly associated with clot stiffness than fibrin, and it appears to be true that thrombi in cancer-related stroke are platelet-rich. Catheters with sizes that update the definition of large bore, such as the AXS Vecta 74 with distal internal diameter of 0.074 inches, are now available for use in the intradural arteries, and contact aspiration with such large-bore catheters can be the key to retrieving highly stiff clots. In Japan, using both a stent retriever and an aspiration catheter to perform combined as-a-unit thrombus retrieval is the mainstream as a first-line technique. In our institution’s data, the combined technique is indeed effective, but its effectiveness is lost in patients with tortuous internal carotid artery. The elongation and flattening of stent retriever in tortuous vessels cannot be compensated even by using the combined technique. A delivery assist catheter AXS Offset should be effective in overcoming the anatomical obstacles to firmly contact a large-bore aspiration catheter to the target clot. The technique selection according to clot architecture and vascular anatomy, which is facilitated by the recent expansion of the lineup of thrombectomy devices, is reviewed from the perspective of an interventional neurologist.
SS5-2 Unfavorable aortic arch anatomy for Mechanical thrombectomy and our bailout.

Hidesato Takezawa\textsuperscript{1,2}, Tetsuya Katsumori\textsuperscript{2}, Hitoshi Kawano\textsuperscript{2}, Takuma Kato\textsuperscript{2}, Daisuke Nakashima\textsuperscript{2}, Manabu Yamamoto\textsuperscript{4}, Yasunori Udura\textsuperscript{4}, Kengo Kishida\textsuperscript{4}, Gaku Manabu\textsuperscript{4}, Shigeomi Yokoya\textsuperscript{4}, Hideki Oka\textsuperscript{4}, Akihiro Fujii\textsuperscript{2}

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Endovascular treatment (EVT) has completely improved the prognosis of acute ischemic stroke (AIS) patients with a proximal intracranial large vessel occlusion (LVO) of the anterior circulation. It is necessary to start EVT instantly and to get recanalization as soon as possible. Society of NeuroInterventional Surgery had set the ideal time from arterial puncture to recanalization (PTR) at 30 minutes. Therefore, in AIS patients with LVO of the anterior circulation, the time from arterial puncture to placement of a large-bore balloon guiding catheter in the target vessel (PTG) should be less than 20 minutes.

We retrospectively studied consecutive 104 acute anterior ischemic stroke patients treated with endovascular therapy in our department during the three years from May 2016 to April 2019. We analyzed the PTG. Only one of the 104 cases failed to have a guiding catheter placed. The median (interquartile range: IQR) age was 80 (73-86) years and 50 cases (49%) were male. The median (IQR) PTG was 12(8-16) minutes. But the PTG in 18 cases (17%) took more than 20 minutes. Among them, 17 cases obtained effective recanalization (TICI: 2b/2c/3), and the median (IQR) PTR was 65.5 (47-100) minutes.

We analyzed the failed case and the 18 cases in which PTG took more than 20 minutes. 9 cases were difficult to place due to anatomical reasons (aortic arch type: 3). 7 cases were right anterior circulation, and 2 cases were left.

Now with the turnover technique, we are able to guide a large-bore balloon guiding catheter into the target vessel more quickly. Here we will present the turnover technique in the patient with aortic arch type: 3. We will also present some of our innovations in EVT for AIS patients with LVO.
SS6 Antagonists to Oral Anticoagulants Now Available: Differences and Tips for Use

Teruyuki Hirano
Professor and Chairman, Department of Stroke and Cerebrovascular Medicine Kyorin University School of Medicine, Tokyo, Japan

According to the Japan Stroke Data Bank 2021, 30% of recent cerebral hemorrhages are related to antithrombotic drugs. Compared to warfarin, the incidence of cerebral hemorrhage is about half during DOAC use, but once it occurs, the mortality rate is similar to that of warfarin. According to the latest guidelines, for cerebral hemorrhage when taking DOACs, the following are indicated: withdrawal, administration of activated charcoal, adequate hypotension, hemostasis, transfusion, and appropriate neutralization. As andexanet alfa was approved in 2022, line up of neutralizers for all kinds of oral anticoagulants including direct thrombin inhibitor, warfarin and Xa inhibitors, is now complete. There are rules for the indications and usage depending on the characteristics of each neutralizing agent. This talk will summarize the differences and tips for the use of antagonists.
In terms of stroke prevention, anticoagulation therapy by using NOACs has become widely used compared to about 10 years ago when the first direct thrombin inhibitor was launched in Japan. In Japan, the number of catheter ablation procedures for patients with atrial fibrillation is increasing year by year, and asymptomatic cerebral infarction found before and after ablation procedures is one of the key topics. A lot of evidence in practice have been accumulated under usage of a reversal agent for direct thrombin inhibitor administration, both in the cerebral and cardiovascular area. In addition, to make anticoagulation therapy safer, we have also conducted educational activities for patients with anticoagulant and their families, such as the “Think FAST” campaign.

On the other hand, 26,300 patients are admitted to the ICU every year in Japan, and the number is increasing every year due to the aging society, though severe brain injury, severe stroke (subarachnoid hemorrhage, cerebral infarction, intracerebral hemorrhage), and epilepsy are generally considered to be rare. This trend is same worldwide, with 82,000 patients admitted to ICUs each year in the United States and 131,000 each year in Europe. Since we cannot expect regeneration and neogenesis of nerve cells in the brain, the most promising treatment is cerebral protection, and therapeutic technologies in this area has made remarkable progress. Multimodal sensors and focal brain cooling (FBC), a method that optimizes brain cooling while simultaneously monitoring numerous brain functions, are expected as further advance therapeutic technologies for a new concept that has the potential to save the lives and suffering of patients with severe brain diseases.
A lot of studies have shown a close association between atrial fibrillation (AF) and vascular dementia. It is apparent that AF is a major risk for stroke, and stroke is the greatest risk for vascular dementia. However, the relationship between Alzheimer’s disease (AD) and AF remains elusive. Several epidemiological studies have shown that AF significantly raises the risk of AD by 1.5- to 2.5-fold. Chronic cerebral hypoperfusion, resulting from persistent AF, could explain the association because hypoperfusion may accelerate senile plaques and amyloid angiopathy by upregulating beta-amyloid-producing enzymes and lowering beta-amyloid clearance efficiency. Furthermore, hypoperfusion may accelerate tau pathology through upregulation of tau-phosphorylating enzymes and via the amyloid cascade. However, most neuropathological studies do not support the direct link between AD pathology and AF but rather suggests vascular neuropathology is related to, or coexistent with, AF and lowers the threshold for clinically-evident AD. The link between AD and AF may be mediated by vascular neuropathology. Observational studies have shown that catheter ablation is associated with less incidence of AD in AF patients, suggesting rhythm-control suppresses hypoperfusion-induced AD neuropathology. In addition, rate-control may also lower the rate of cognitive decline in cognitively impaired elderly subjects with AF. Further studies are warranted to clarify the mechanisms underlying the link between AF and AD. However, anticoagulation and rhythm- or rate-control against AF may hold promise even for AD patients.
Hypertension is common, has a high attributable risk for stroke (25%–50%), and many clinical trials have shown that blood pressure-lowering therapy (BPL) can reduce the risk of first and recurrent stroke. Recently, intensive BPL has been associated with reduction in the risk of dementia and mild cognitive impairment.

In acute ischemic stroke, there had been a concern that cerebral blood flow decreases due to hypotension, leading to the expansion of infarction. The CATIS trial demonstrated the safety of BPL below 140/90 within 7 days of onset of stroke. In addition, with the spread of reperfusion therapy, BPL after recanalization is required for preventing intracranial hemorrhage. However, the ENCHANTED and BP-TARGET trials have shown that intensive BPL after reperfusion therapy does not improve outcomes, suggesting that moderate BPL should be used after reperfusion therapy.

In acute intracerebral hemorrhage, a meta-analysis of 6 RCTs showed that intensive BPL was not significantly effective in reducing hematoma growth and poor outcome, but was safe. In addition, BPL may be effective in young people, early onset cases, and cases with small hematomas at the onset.

In secondary stroke prevention, a meta-analysis of 4 RCT showed that intensive BPL reduce the risk of stroke recurrence by 22%, and the risk of intracerebral hemorrhage by 75%. In Asians, small vessel diseases, including lacunar infarction and intracerebral hemorrhage, are common stroke subtype and the frequency of having deep type cerebral microbleeds is high. When antithrombotic therapy is given to such patients, the risk of intracerebral hemorrhage should be particularly concerned, and a strict BPL less than 130/80 is important.
High-score abstracts (Best presentation award)

HA-1 RNF213 p.R4810K variant predicts long-term progression of intracranial artery stenosis: A 15-year follow-up study

Shuhei Okazaki¹, Takeshi Yoshimoto², Mariko Ohara¹, Masatoshi Takagaki³, Kotaro Watanabe¹, Yasufumi Gon¹, Kenichi Todo¹, Tsutomu Sasaki¹, Hiroyuki Araki⁴, Tomomi Yamada⁵, Shirou Manabe⁶, Hajime Nakamura³, Haruhiko Kishima³, Masafumi Ihara², Hideki Mochizuki¹

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⁶Department of Medical Informatics, Osaka University Graduate School of Medicine, Osaka, Japan

Background and Purpose: Intracranial artery stenosis is the predominant etiology of ischemic stroke in the Asian population. Further, the presence of the RNF213 p.R4810K variant, which is a susceptibility gene for moyamoya disease, increases the risk of ischemic stroke attributable to large-artery atherosclerosis. Accordingly, we hypothesized that this genetic variant may affect the long-term outcome of intracranial artery stenosis in the East Asian population. We thus aimed to examine the effect of this variant on the long-term progression of intracranial artery stenosis.

Methods: Using a prospective database, we identified adult patients with intracranial artery stenosis who underwent periodic magnetic resonance imaging (MRI) examinations for > 5 years. We evaluated stenosis progression using a validated visual grading system. We excluded patients diagnosed with moyamoya disease at the time of initial MRI. Genotyping of RNF213 p.R4810K was performed at the end of the follow-up period.

Results: Among 52 eligible patients, 22 (42%) were carriers of the RNF213 p.R4810K variant. The median follow-up duration was 10.3 years. Two variant carriers were newly diagnosed with moyamoya disease. There was a significant association of the RNF213 p.R4810K variant with time to progression of intracranial artery stenosis (log-rank P = 0.004, Fig-A). Progression of intracranial stenosis was significantly less frequent among patients who received statins (Fig-B). Stratification according to the RNF213 p.R4810K variant revealed a significant risk reduction by statin treatment in variant carriers but not in non-carriers (Fig-C, D). In a multivariate Cox regression model adjusted for age and sex, the non-use of statins and the RNF213 p.R4810K variant carrier status were independent predictors of the progression of intracranial artery stenosis.

Conclusion: Our findings indicated that the RNF213 p.R4810K variant increases the risk of intracranial artery stenosis progression. Statin treatment may prevent the progression of intracranial artery stenosis.
High-score abstracts (Best presentation award)

**HA-2 Underweight predicts poststroke cardiovascular events in patients without atrial fibrillation**

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**Background and purpose:** We were aimed to know whether underweight is associated with poststroke cardiovascular events, and whether the association is different according to the presence of atrial fibrillation (AF).

**Methods:** We studied the patients with acute stroke or transient ischemic attack who were prospectively registered in multicenter stroke database from Apr 2008 to Jul 2020, excluding those aged 75 or older and those over normal weight. We prospectively captured major adverse cardiovascular events (MACE) within 1 year after stroke. Cox-proportional hazard regression were conducted in each subgroup with and without AF adjusting for predetermined vascular risk factors and potential confounders.

**Results:** Among 30,912 patients, 1,494 (4.8%) cases were underweight and 29,418 (95.2%) cases were normal weight. The cumulative event rate of 1-year MACE was higher in the underweight (9.0%) than in the normal (5.6%). In Cox-proportional regression, underweight was associated with significantly higher MACE (adjusted hazard ratio [HR] 1.62, 95% confidence interval [CI] 1.26-2.09) and recurrent stroke (adjusted HR: 95% CI 1.42, 1.02-1.98) in all study patients. In patients with AF, the risk of MACE for the underweight was not significantly increased. In contrast, in patients without AF, the underweight had a consistently higher risk of MACE (adjusted HR 1.66, 95% CI 1.25-2.22) and recurrent stroke (adjusted HR 1.50, 95% CI 1.05-2.14).

**Conclusions:** Underweight increased the risk of MACE and recurrent stroke within 1 year after acute stroke, especially in stroke without AF.
Background and Purpose: To investigate the association between vascular risk factors and progression of cerebral small vessel burden on brain magnetic resonance imaging (MRI) in neurologically healthy adults.

Methods: Among consecutive adults who underwent brain health examinations including MRI between December 2005 and November 2011, those who underwent follow-up MRI at least 1 year after the initial MRI were considered as candidates for analysis. Initial and follow-up MRI were performed on the same equipment using the same protocol. The presence of features of cerebral small vessel disease (SVD), including lacunes, cerebral microbleeds, white matter changes, and basal ganglia perivascular spaces were summed to obtain “total SVD score” (range, 0–4). Progression of SVD was defined as a ≥1 point increase in total SVD score at follow-up relative to baseline. Multivariate logistic regression analyses were performed to investigate the association of progression of SVD with demographic vascular risk factors and with clinical characteristics at baseline. Sensitivity analyses were conducted similarly in middle-aged participants (aged 45-65 years) and to determine the risk factors for total SVD score ≥ 2 among participants with an initial score of ≤1.

Results: Included were 674 neurologically healthy adults (mean age, 57.8 years at baseline; 49% male) and the mean follow-up period was 7.0 years. Progression of SVD was observed in 154 subjects (22.8%). Multivariate logistic regression analyses showed that progression of SVD was associated with age (per 10-year increase, odds ratio [OR]: 1.88, 95% confidence interval [CI] 1.48–2.39), hypertension (OR 1.51, 95%CI 1.03–2.21), systolic blood pressure (per standard deviation [SD] increase, OR 1.26, 95%CI 1.04–1.53), and mean arterial pressure (per SD, OR 1.24, 95%CI 1.02–1.51). These findings remained robust in sensitivity analyses.

Conclusions: Aging and hypertension appear to play a key role in the progression of cerebral small vessel burden after mid-life.
### HA-4  The predictive role of CHA2DS2-VASc score between venous thromboembolism and ischemic stroke: the good, the bad and the unknown

Wei Syun Hu  
Department of cardiology, cmuh Taiwan

**Purpose:** This study aimed to explore the predictive role of CHA2DS2-VASc score between venous thromboembolism (VTE) and ischemic stroke.

**Methods:** The current study was analyzed from the in-patient claims data of the Taiwan National Health Insurance Research Database. We identified the patients diagnosed with VTE (for Study 1) or ischemic stroke (for Study 2) from 1 January 2000 to 31 December 2011 to observe the occurrence of ischemic stroke (for Study 1) and VTE (for Study 2), respectively. We used the CHA2DS2-VASc score to evaluate the risk of ischemic stroke among VTE patients (for Study 1) and to measure the risk of VTE among ischemic stroke patients (for Study 2). The predictive ability of CHA2DS2-VASc score was assessed by C-statistics based on Cox-regression analysis and receiver-operating characteristic (ROC) curve analysis.

**Results:** A total of 56,996 patients with VTE (Study 1), whereas a total of 688,556 patients with ischemic stroke (Study 2) were identified. The C-statistics of the CHA2DS2-VASc score for predicting ischemic stroke among VTE patients and for predicting VTE events in patients with ischemic stroke were 0.71 [95% confidence interval (CI) = 0.70-0.72] and 0.61 (95% CI = 0.60-0.62), respectively. Furthermore, among VTE patients, the area under the curve of ROC of CHA2DS2-VASc score predictive of ischemic stroke was 0.66 (95% CI = 0.65-0.67), whereas the area under the curve of ROC of the score predictive of VTE was 0.55 (95% CI = 0.54-0.55) in patients with ischemic stroke.

**Conclusion:** Our study is the first to concern the performance of CHA2DS2-VASc score in predicting the risk of ischemic stroke in VTE patients and the risk of VTE in ischemic stroke patients. Nevertheless, the performance of the score was modest, and the transportability of the score in these populations still needs to be defined.
High-score abstracts (Best presentation award)


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To examine the efficacy of stereotactic radiosurgery (SRS) or SRS with embolization (Emb-SRS) for dural arteriovenous fistulas (DAVs), we conducted a multi-institutional retrospective study including 13 Japanese gamma knife centers. Two-hundred patients with DAVF treated with SRS or Emb-SRS were analyzed to examine fistula obliteration rate, factors associated with obliteration, and differences between SRS and Emb-SRS. The 3- and 4-year obliteration rates were 66.3% and 78.8%, respectively, with the post-SRS hemorrhage rate being 2% (4/200). Symptomatic adverse radiation events were observed in two patients (1.0%). Disease-specific mortality was not observed. Multivariate Cox proportional hazard analysis demonstrated that DAVF location and absence of cortical venous reflux (CVR) were significantly associated with obliteration. Propensity score matching was performed to examine the effect of embolization, revealing that the rates of obliteration or post-SRS hemorrhage were not different between SRS and Emb-SRS. A radiosurgical grading system was created using the significant factors in the multivariate analysis (location category [2 points for anterior or middle skull base (lowest expectation), 1 point for superior sagittal sinus/tentorial (intermediate expectation), and 0 point for cavernous sinus/transverse-sigmoid/others (highest expectation)] and CVR [1 point for presence of CVR]), based on which patients were stratified into three groups; for patients with highest (0 point), intermediate (1 point), and lowest (2 points or higher) expectations, the 4-year obliteration rates were 94.4%, 71.3%, and 60.4%, respectively (P < 0.01). In conclusion, SRS alone or Emb-SRS can be safely performed for DAVFs. The likelihood of obliteration can be predicted using the new grading system. The results may help surgeons determine more appropriate therapeutic strategies for DAVFs.

![Graph (A)](image1.png)

**Graph A: Radiosurgical grading system.**

<table>
<thead>
<tr>
<th>CVR</th>
<th>Fistula location</th>
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<tr>
<td>Present</td>
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<tr>
<td>SSS or tentorium</td>
<td>1 point</td>
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<tr>
<td>ASI or MF</td>
<td>2 point</td>
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<table>
<thead>
<tr>
<th>Total points</th>
<th>Obliteration rate</th>
<th>Significance</th>
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<tbody>
<tr>
<td>0</td>
<td>Highest expectation group</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>1</td>
<td>Intermediate expectation group</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>≥2</td>
<td>Lowest expectation group</td>
<td>P &lt; 0.01 (for the entire model)</td>
</tr>
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![Graph (B)](image2.png)

**Graph B: Follow-up months from SRS.**
HA-6 Risk of dementia according to the smoking habit change after ischemic stroke: a nationwide population-based cohort study

Minwoo Lee¹, Kyung Ho Yu¹, Jae-Sung Lim²
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²Department of Neurology, Asan Medical Center, Seoul, Korea

Objective
We investigated the effects of smoking habit change on the risk of incident dementia in the ischemic stroke population using the Korean National Health Insurance Services Database.

Methods
This Nationwide population-based cohort study included 197,853 patients with ischemic stroke. The subjects were divided into never smokers, former smokers, smoking quitters, sustained smokers, and new smokers, based on the 2-year change in smoking status between the first and second health examinations. The subjects were followed from the index date to 2018 to assess the development of dementia. Dementia was further categorized into Alzheimer’s disease dementia and Vascular Dementia according to the ICD-10 diagnosis. Multivariate Cox proportional models were used to assess the effects of smoking habit change on the risk of dementia.

Results
After a median of 4.04 years of follow-up, a total of 19,595(9.9%) dementia cases were observed. Among them, 15189(7.7%) were diagnosed with AD and 2719(1.4%) patients with VaD. After adjusting for covariates including age, sex, habits of alcohol intake and physical activity, income, history of hypertension, diabetes, dyslipidemia, chronic kidney disease, and cigarette pack-year, new smokers, sustained smokers, and smoking quitters were significantly associated with a higher risk of any dementia compared to never smokers. (aHR 1.395; 95% CI 1.254-1.552, aHR 1.324; 95% CI 1.236-1.418, and aHR 1.170; 95% CI 1.074-1.275, respectively). Similar trends were observed in both AD and VaD, but the effects of new smokers on VaD were not significant. The impact of smoking habit change was more prominent among the 40-65 years group and in low-income group.

Conclusion
In this large nationwide cohort study, new smokers and sustained smokers had a significantly higher risk of incident dementia after ischemic stroke. Smoking quitters also had an elevated risk of incident dementia, but the detrimental effects were lower than in new smokers and sustained smokers.
On-demand oral presentation

O-1 Lactate and lactate dehydrogenase in carotid cistern as biomarkers of early brain injury and delayed cerebral ischemia of aneurysmal subarachnoid hemorrhage

Mitsuhiro Anan1,2, Kunpei Takao1, Wataru Matsushita1, Daigo Aso1, Hirotaka Fudaba1, Kouhei Onishi1, Hiroyuki Matsuta1, Kenji Sugita1, Takeshi Matsuda2, Takeshi Kubo1, Yasuyuki Nagai2,3, Minoru Fujiki1

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Objective: The pathophysiology of delayed cerebral ischemia (DCI) following aneurysmal subarachnoid hemorrhage (aSAH) has not been fully evaluated. The aim of this study was to evaluate the dynamics of lactate and lactate dehydrogenase (LDH) in carotid cisternal cerebrospinal fluid (CSF), and to discuss their effectiveness as markers of early brain injury (EBI) and DCI following aSAH.

Patients and Methods: Among 91 consecutive aSAH patients treated between January 2012 and March 2019 at National Hospital Organization Beppu Medical Center, 19 patients (20.9%) were eligible for this retrospective study. Concentrations of lactate and LDH in carotid cisternal CSF within 14 days after onset of aSAH were evaluated.

Results: Six of the 19 patients (31.6%) had a history of DCI. Both lactate and LDH levels in carotid cisternal CSF were significantly higher in the DCI group than in the non-DCI group on postbleeding day (PBD) 1-2, 3-4, and 5-6. Interestingly, neither lactate nor LDH levels in blood differed significantly between DCI and non-DCI groups on PBD 1-2.

Conclusions: Lactate and LDH concentrations in carotid cisternal CSF may vividly reflect the EBI and may thus represent predictive biomarkers of DCI following aSAH.
### On-demand oral presentation

<table>
<thead>
<tr>
<th>O-2</th>
<th>Intraarterial therapy of Rho-kinase inhibitor following mechanical thrombectomy for acute ischemic stroke</th>
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<td>Yoichi Morofuji¹, Shinsuke Nakagawa², Kazuaki Okamura¹, Kei Sato¹, Tsuyoshi Izumo¹, Takayuki Matsuo¹</td>
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<td>¹Department of Neurosurgery, Nagasaki University, Nagasaki, Japan, ²Department of Pharmacology, Fukuoka University, Fukuoka, Japan</td>
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Attempts to develop new drugs for acute ischemic stroke are still struggling; however, mechanical thrombectomy is now at the forefront of the treatment of large-vessel acute ischemic stroke. Selective intra-arterial access has opened a new avenue for neuroprotection in acute ischemic stroke that has the potential to maximize the local benefits while minimizing systemic effects. We investigated the effect of fasudil, rho-kinase inhibitor, on blood-brain barrier (BBB) against ischemia-reperfusion injury. We used in vitro BBB models with rat primarily cultured brain capillary endothelial cells, astrocytes and pericytes, and subjected cells to either normoxia or 6-h oxygen glucose deprivation (OGD)/24-h reoxygenation. Fasudil inhibited the decreases in TEER induced by 6-h OGD/24-h reoxygenation and decreased the endothelial permeability for sodium fluorescein through the BBB model. Immunocytochemical and western blot analyses showed that fasudil increased the expression of claudin-5, the main functional protein of tight junctions under 6-h OGD/24-h reoxygenation as well as normoxia. Our data indicate that rho-kinase inhibitor fasudil strengthens the barrier integrity in BBB. Since mechanical thrombectomy is now the gold standard for acute ischemic stroke treatment, neuroprotective strategies via the intra-arterial route during mechanical thrombectomy are highly anticipated.
On-demand oral presentation

**0-3 Neuropathological analysis of COVID-19: An autopsy study of four cases**

Terunori Sano¹, Masashi Mizutani¹, Yuji Nakayama¹, Hiroaki Kimura², Masayuki Ohira³, Yuji Saitoh¹, Hajime Ariga², Koji Abe³, Masaki Takao¹

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³Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry, Tokyo, Japan

Patients infected with SARS-CoV-2 demonstrate a wide spectrum of neuropsychiatric symptoms. Cerebrovascular diseases have been reported to be the most common neuropathological finding in autopsies. We examined the neuropathologic findings of stroke in the acute phase of COVID-19 using autopsy cases. From April 2021 to March 2022, we examined four COVID-19 autopsy cases. The neuropsychiatric clinical diagnoses were as follows: schizophrenia in two patients, vascular dementia in one, and frontotemporal dementia in one. The ages of the patients ranged from 68 to 77 years. COVID-19 disease duration ranged from 10 to 20 days. Two patients were male. In all cases, at the time of autopsy, polymerase chain reaction for SARS-CoV-2 RNA using swabs of cerebrospinal fluid yielded negative results. All patients had died of pneumonia. Recent multiple cerebral small infarcts with microthrombi in the vessel were found in three patients, with accompanying multiple old infarcts in one patient. One patient showed subacute cerebral small infarcts. It is said that COVID-19 predisposes patients to coagulation abnormality and infarctions, including those of the central nervous system. In patients with COVID-19, the risk of chronic and acute strokes should be considered. Because our sample size was small, further analysis involving autopsy cases is needed to clarify the neuropathology of COVID-19.
**Purpose:** The relation between hospitalization timing and risk of clinical outcomes among patients with atrial fibrillation (AF) with and without stroke remained undetermined.

**Methods:** Rehospitalization due to AF, cardiovascular (CV) death and all-cause mortality were the outcomes of interest in this study. Multivariable Cox proportional hazard model was applied to estimate the adjusted hazard ratio (HR) and 95% confidence interval (CI).

**Results:** While considering patients with AF hospitalized during weekdays without stroke as the reference group, patients with AF hospitalized during weekends with stroke had the risk of AF rehospitalization, CV death and all-cause death by 1.48 (95% CI 1.44 to 1.51), 1.77 (95% CI 1.71 to 1.83) and 1.17 (95% CI 1.15 to 1.19) times, respectively.

**Conclusion:** Patients with AF hospitalized during weekends with stroke had the worst clinical outcomes.
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On-demand oral presentation

**O-7 Epilepsy in stroke patients**

Jun Hong Lee¹, Sung-Hee Hwang²

¹Department of Neurology, National Health Insurance Service Ilsan Hospital, Goyang-si, Korea,
²Department of Neurology, Hallym University Kangnam Sacred Heart Hospital, Seoul, Korea

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**Introduction:**
The incidence of epilepsy in elderly stroke patients has been significant attention because planning future needs for health services and improved primary and secondary prevention of stroke are important. We evaluated the relationship between stroke and the subsequent development of epilepsy within 10 years follow-up.

**Methods:**
This retrospective, nationwide, longitudinal study used National Health Insurance Service -Senior cohort (NHIS-Senior) comprising 550,000 random subjects who were selected from over than 60 years old. This study included a cohort of 42,925 patients who were first diagnosed as stroke between 2009 and 2011. To match each stroke patient, 218,478 control subjects were selected from the database.

**Results:**
In this cohort, the prevalence of stroke was higher in female(62%) than in male(38%). A higher prevalence of stroke was observed in the 60-70 years age and more than 80 years age group in urban area. The incidence of stroke was increased from 2002 to 2009, but decreased from 2010 to 2013. The diagnosis of epilepsy was done at averagely 20 months after the diagnosis of stroke. Cox regression analysis showed that the HR of epilepsy was 7.658 times greater for patients with stroke (95% CI: 7.402-7.923) than for control group after adjusting for other risk factors. The HR of epilepsy was 1.08 (95% CI: 1.045-1.116) in female patients, 1.66(95% CI: 1.607-1.715) in diabetic patients, 1.679(95% CI: 1.625-1.734) in hypertensive patients, 1.831(95% CI: 1.626-2.062) in chronic kidney disease and 1.647(95% CI: 1.593-1.703) in hypercholesterol patients.

**Conclusions:**
Our findings suggest that stroke may be an independent risk factor for epilepsy in elderly patients(HR 7.658, 95% CI: 7.402-7.923). So we need to control and pay attention to epilepsy in elderly stroke patients.
**On-demand oral presentation**

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<th>Long-term incidence of major gastrointestinal bleeding in acute ischemic stroke</th>
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<td>Jun Yup Kim, Beom Joon Kim, Jihoon Kang, Seong-Eun Kim, Hee-Joon Bae</td>
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<td>Department of Neurology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea</td>
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**Backgrounds:** Incidence of major gastrointestinal bleeding (GIB) required blood transfusion after acute ischemic stroke (AIS) was reported as 0.5% during hospitalization. However, it is not known about the long-term incidence rates by period after AIS.

**Methods:** AIS patients who were admitted to the 14 hospitals between 2011 and 2013 were identified using a nationwide multicenter prospective stroke registry database. GIB was captured with diagnosis codes through linkage between registry and claims data. GIB requiring at least 2 packs of blood transfusion was defined as major GIB. Incidence rates were calculated for each epoch: 0-30 days, 31-90 days, 91-180 days, 181-365 days, 1-2 years, 2-3 years, after 3 years.

**Results:** Of 10,818 AIS patients (male, 59%; age, 68±13 years), 947 patients (8.8%) had 1,224 episodes of major GIB during median follow-up of 3.1 years. Twenty percent of these 947 had ≥2 bleeding episodes. The second bleeding occurred mostly within a month of the first. The incidence rates were highest in the first month with 19.21 per 100 person-years, and gradually decreased to about 1/6 at the first year, and then showed plateau above 3 years. In the multivariable recurrent event analysis, anemia at admission, lower eGFR below 60, and 3-month mRS ≥4 were independently associated with higher risk of major GIB during the observation periods.

**Conclusions:** Major GI bleeding occur frequently after AIS in the first month, and the risk was gradually decreased. The efforts are needed to prevent it, especially in patients with anemia and decreased renal function.
On-demand oral presentation

**0-9 White matter hyperintensity load aggravates functional outcome after mild ischemic stroke, but probably not after moderate-to-severe ischemic stroke**

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**Background**
White matter hyperintensity (WMH) is associated with post-stroke functional outcomes. However, it is uncertain whether the prognostic power of WMH differs depending on the severity of ischemic stroke.

**Objective**
To assess stroke severity-related differences in the strength of the association between WMH volume quintiles and post-stroke functional outcome at 3 months using a nationwide imaging-based stroke database.

**Methods**
From May 2011 to February 2014, we screened 14,070 consecutive patients with acute ischemic stroke who visited 11 participating centers within 7 days of symptom onset. Mild stroke was defined as magnetic resonance imaging (MRI)-confirmed ischemic stroke with the baseline National Institute of Health Stroke Scale (NIHSS) scores of 1-4, and moderate-to-severe stroke as the one with the baseline NIHSS score of ≥5. WMH volume (% of the parenchymal brain volume) was measured and categorized into quintiles. To examine if higher WMH quintiles are associated with poor 3-month functional outcome (modified Rankin Scale score of ≥3) differently in mild vs. moderate-to-severe strokes, multivariable logistic regression analysis including an interaction term (WMH burden × stroke severity) was performed.

**Results**
Mean age of 8,918 enrolled patients was 67.2±12.6 years, and 60.1% (n=5,362) men. The association between WMH quintiles and poor functional outcome at 3-month was significantly modified by stroke severity (P-for-interaction < 0.001). In mild stroke (n = 4,994), WMH quintiles were associated with poor 3-month functional outcome in a dose-dependent manner (Table). In moderate-to-severe stroke (n = 3,924), however, there seemed to be a threshold effect: the highest WMH quintile was significantly associated with poor functional outcome (adjusted odds ratio 1.67, 95% confidence interval 1.20-2.20, P<0.001), whereas the second to fourth WMH quintiles were not (all P > 0.05; Table).

**Conclusion**
WMH load aggravates 3-month functional outcome after mild ischemic stroke, but probably not after moderate-to-severe ischemic stroke.
**On-demand oral presentation**

### O-10 Comparison of hospital performance rankings in acute ischemic stroke care based on mortality- vs functional outcome-based measures

Bosco Seong Kyu Yang¹, Beom Joon Kim¹, Moon-Ku Han¹, Hee-Joon Bae¹, Joon-Tae Kim², Jae-Kwan Cha³, Dong-Eog Kim⁴, Jong-Moo Park⁵, Kyusik Kang⁶, Soo Joo Lee⁷, Byung-Chul Lee⁸, Keun-Sik Hong⁹, Jay Chol Choi¹⁰, Tai Hwan Park¹¹, Kyung Bok Lee¹², Jee-Hyung Kwon¹³, Sung Il Sohn¹⁴, Jun Lee¹⁵, Ji Sung Lee¹⁶, Juneyoung Lee¹⁷

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**Introduction**

Recent evidence suggests the potential correlation between the modified Rankin scale (mRS)—the standard outcome measure used in acute stroke care—and mortality-based measures, which are frequently used by health agencies in evaluating hospital performance. This study attempts to examine whether the two measures are interchangeable in evaluating hospital performance.

**Method**

Five different outcome measures—unfavorable outcome (three-month mRS ≥ 2), death or dependency (three-month mRS ≥ 3), one-month mortality, three-month mortality, and one-year mortality—were collected for each acute stroke patient admitted to the hospitals participating in the CRCS-K registry. Hierarchical regression models were used to calculate per-hospital risk-adjusted outcome rates (RAOR) for each measure. Hospitals were ranked based on RAORs, and the rankings were analyzed for correlations and agreements in grouping capacities.

**Result**

Comparison between the rankings based on unfavorable outcome and one-year mortality resulted in Spearman correlation coefficient and Kendall rank coefficient of -0.29 and -0.23, and the comparing grouping capacities using two different grouping systems (top 33%/middle 33%/bottom 33% and top 20%/middle 60%/bottom 20%) resulted in weighted kappa of 0.125 and 0.25. No significant correlation or similarity in grouping capacities were found between the rankings based on functional outcome measures and those based on mortality-based measures.

**Conclusion**

Mortality-based measures may not be suitable substitutes for functional outcome-based measures in evaluating hospital performance.
On-demand oral presentation

**0-11  Factors associated with physical activity and sedentary behavior among community-dwelling stroke survivors**

Eung-Joon Lee, Han-Yeoung Jeong, Keun-Hwa Jung
Department of Neurology, Seoul National University Hospital, Seoul, Korea

### Background and Aims
Although insufficient physical activity (PA) and sedentary behavior (SB) are established independent risk factors for stroke, stroke survivors may be at a higher risk of physical inactivity. Thus, we investigated the factors associated with PA and SB of stroke survivors in a community setting.

### Methods
A cross-sectional study was performed using representative data from the Korea National Health and Nutrition Surveys from 2016 to 2020. We compared the level of moderate to vigorous aerobic PA, resistance exercise, and sedentary time between stroke survivors and controls. Then we performed a multivariate analysis to investigate the factors associated with physical inactivity and long sedentary time. The recommended level of aerobic PA was at least 150 min of moderate-intensity activity or at least 75 min of vigorous-intensity activity or an equivalent combination of moderate and vigorous-intensity activity throughout the week. The sufficient level of resistance exercise was defined as ≥2 days/week. Long sedentary time was defined as spending ≥8 h/day on SB.

### Results
Physical inactivity was significantly more prevalent among stroke survivors. The older age (odds ratio [OR]=5.448, p=0.001), and living in rural areas (OR=1.911, p=0.020) were associated with low levels of aerobic PA. Female sex (OR=0.427, p=0.007) was associated with a low degree of resistance exercise. Finally, living without economic activity (OR=2.224, p=0.001), subjective unhealthy (OR=1.458, p=0.027), a single life (OR=1.611, p=0.049), and old age (OR=1.231, p=0.046) were independent predictors of long sedentary time.

### Conclusions
Based on these results, further research and policy studies are needed to increase the physical activity of stroke survivors.
On-demand oral presentation

0-12 Amplified risk of intracranial artery stenosis in familial hypercholesterolemia by RNF213 p.R4810K

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Introduction: The relationship between familial hypercholesterolemia (FH) and cerebrovascular diseases remains to be elucidated. The RING finger protein 213 gene (RNF213) p.R4810K variant is associated with Moyamoya disease in East Asian people, and is also regarded as a strong genetic risk factor for development of intracranial major arterial stenosis/occlusion (ICASO) in the anterior circulation. However, the p.R4810K is also observed in 2-3% of the general population; only 1 in 50 variant carriers develop ICASO. Therefore, additional factors should be required for the variant carriers to develop ICASO. We aimed to investigate whether the RNF213 p.R4810K affects the prevalence of ICASO in FH patients.

Methods: We enrolled 167 patients who were diagnosed with FH and underwent brain magnetic resonance imaging (MRI) at our hospital from May 2005 to June 2021. We evaluated RNF213 p. R4810K variant, and LDLR and PCSK9 gene mutations, and analyzed frequency of ICASO in brain MR angiography.

Results: The RNF213 p. R4810K was found in 6 FH patients (3.6%). Five of the six variant carriers (83.3%) showed ICASO in the anterior circulation, with a significant difference in the frequency of ICASO between the variant carriers and non-carriers (p = 0.027). Also, the logistic regression analysis showed that carrying RNF213 p.R4810K was a significant predictor for ICASO development in the anterior circulation among the FH patients (logistic regression: OR 21.58, 95% CI 2.60–480.61, p = 0.012; exact-like inference: OR 7.91, 95% CI 1.94–∞, p = 0.013). The median number of stenotic or occluded arteries in the anterior circulation was also significantly larger in the variant carriers (2.5 vs. 0, p = 0.01).

Discussion: FH patients showed higher prevalence and severity of ICASO associated with RNF213 p.R4810K. Gene mutations for FH and/or prolonged dyslipidemia may confer a high risk of ICASO in the RNF213 p.R4810K carriers.
On-demand oral presentation

O-13  Increased cerebral small vessel disease burden with renal dysfunction and albuminuria: the BAT2

Kanta Tanaka1, Kaori Miwa1, Masahito Takagi1, Makoto Sasaki2, Yusuke Yakushiji3,4, Kohsuke Kudo6, Masayuki Shiozawa1, Jun Tanaka3, Masashi Nishihara6, Yoshitaka Yamaguchi7, Kyohei Fujita6, Yuku Honda6, Hiroyuki Kawano6, Toshihiro Ide3, Sohei Yoshimura1, Masatoshi Koga1, Teruyuki Hiranò5, Kazunori Toyoda1

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9Department of Stroke and Cerebrovascular Medicine, Kyorin University, Mitaka, Japan

Background and Purpose:
The aim of this study was to determine the associations of cerebral small vessel disease (SVD) burden with renal dysfunction and albuminuria in patients taking oral antithrombotic agents.

Methods:
Patients who newly started or continued taking oral antiplatelets or anticoagulants were enrolled in a prospective, multicenter, observational study. Obligatorily acquired multimodal MRI at registration with prespecified imaging conditions was assessed for cerebral microbleeds, white matter hyperintensities (WMH), enlarged basal ganglia perivascular spaces (BG-PVS), or lacunes, and a total SVD score was calculated (range 0–4). Multivariable adjusting covariates were age, sex, hypertension, diabetes mellitus, dyslipidemia, current smoking, drinking and estimated glomerular filtration rate (eGFR).

Results:
Of 5324 patients (1762 females; median age, 73 years), 4797 (90.1%) patients were taking oral antithrombotic agents for secondary stroke prevention. Cerebral microbleeds were present in 32.7%, confluent WMH in 51.8%, extensive BG-PVS in 38.9%, and lacunes in 59.4%. Median SVD score was 2. Advanced age, hypertension, lower eGFR, and higher urinary albumin-to-creatinine ratio (ACR) constituted risk factors for increased SVD scores (Figure). Compared to eGFR category G1 (eGFR ≥90 mL/min/1.73 m²), adjusted odds ratios for SVD score increment were 1.63 (95% confidence interval [CI], 1.11–2.39) at category G4 (eGFR 15–<30 mL/min/1.73 m²) and 2.05 (95% CI, 1.33–3.16) at G5 (eGFR <15 mL/min/1.73 m²). Corresponding odds ratios relative to ACR category A1 (ACR <30 mg/g) were 1.29 (95% CI, 1.12–1.49) for category A2 (ACR 30–<300 mg/g) and 1.37 (95% CI, 1.05–1.77) for A3 (ACR ≥300 mg/g). When combined eGFR and ACR categories were assessed, risks for SVD score increment generally increased as eGFR decreased and ACR increased.

Conclusions:
Both reduced eGFR and albuminuria were independently associated with increased cerebral SVD burden in patients requiring oral antithrombotic medication mainly for secondary stroke prevention.

Trial Registration Information:
On-demand oral presentation

0-14 Decrease in serum uric acid levels is associated with unfavorable outcomes after ischemic stroke

Kuniyuki Nakamura¹, Kana Ueki¹,², Ryu Matsuo¹,²,³, Takuya Kiyohara¹, Fumi Irie¹,², Yoshinobu Wakisaka¹, Tetsuro Ago¹, Masahiro Kamouchi²,³, Takanari Kitazono¹,³

¹Department of Medicine and Clinical Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan,
²Department of Health Care Administration and Management, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan,
³Center for Cohort Studies, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Background

Serum uric acid (UA) levels have an unfavorable effect on ischemic stroke development. After the stroke onset, serum UA levels have been reported to change significantly. However, their impact on functional outcomes is still unclear. We aimed to investigate the association between changes in serum UA levels and clinical outcomes after acute ischemic stroke using a large-scale, multi-center stroke registry.

Methods

In total, 4,621 previously independent acute ischemic stroke patients from the Fukuoka Stroke Registry in Japan were included. The decrease in serum UA levels during hospitalization was categorized into sex-specific quartile (Q1, no change or increased after admission; Q4, most decreased). The study outcomes were poor functional outcome (modified Rankin Scale score 3–6) and functional dependence (modified Rankin Scale score 3–5) at 3 months. We also evaluated neurological recovery and neurological deterioration using changes in the NIHSS score during hospitalization. Logistic regression analysis was used to evaluate the association of serum UA levels decrease with clinical outcomes.

Results

The frequency of poor functional outcome at 3 months after stroke onset was lowest in the Q1 quartile and highest in the Q4 quartile. The odds ratio for poor functional outcome at 3 months was significantly higher in the Q4 quartile (2.66 [95% confidence interval 2.05–3.44]) than that in the Q1 quartile (reference) after adjustment for confounding factors. Likewise, the Q4 quartile demonstrated the association with functional dependence (2.61 [2.00–3.42]), neurological recovery (0.66 [0.54–0.79]), and neurological deterioration (2.85 [2.02–4.02]), respectively. No heterogeneity was observed according to age, sex, stroke subtype, neurological severity, obesity, chronic kidney disease, or serum UA levels on admission.

Conclusions

Decrease in serum UA levels was independently associated with unfavorable outcomes, including poor functional outcome, functional dependence, poor neurological recovery, and neurological deterioration, in patients after acute ischemic stroke.
**On-demand oral presentation**

**O-15  Rupture of vertebral artery dissecting aneurysm after mRNA anti-COVID-19 vaccination: A report of two cases**

Kohei Chida, Tatsuhiko Talahashi, Suguru Igarashi, Kentaro Fujimoto, Yasushi Ogasawara, Shunrou Fujiwara, Takahiro Koji, Yoshitaka Kubo, Kuniaki Ogasawara

Department of Neurosurgery, Iwate Medical University, Shiwa-gun, Japan

The coronavirus disease 2019 (COVID-19) pandemic continues to spread around the world, and widespread vaccination is considered the most effective way to end it. Although the efficacy of COVID-19 vaccines has been confirmed, their safety remains a concern. In this paper, we report two cases of ruptured vertebral artery dissecting aneurysm (VADA) immediately after messenger RNA (mRNA) anti-COVID-19 vaccination. In Case 1, a 60-year-old woman experienced sudden headache 3 weeks before her first dose of the Moderna mRNA-1273 COVID-19 vaccine. Magnetic resonance imaging showed dilatation of the right vertebral artery (VA) without intracranial hemorrhage. A day after the vaccination, she developed subarachnoid hemorrhage with pulmonary effusion due to a ruptured right VADA. She underwent endovascular internal trapping and parent artery occlusion under general anesthesia. In Case 2, a 72-year-old woman with a previous history of the left VA occlusion due to arterial dissection developed subarachnoid hemorrhage 7 days after the first dose of the Pfizer-BioNTech BNT162b2 COVID-19 mRNA vaccine due to a ruptured right VADA and underwent stent-assisted coil embolization under general anesthesia. The postoperative courses of these two cases were uneventful. The accumulation of more cases and further study are warranted to clarify the relationship between COVID-19 mRNA vaccination and ruptured intracranial dissecting aneurysms.
On-demand oral presentation

O-16  Clinical study of thirteen patients with spinal cord infarction

Katsuhiko Ogawa, Takayoshi Akimoto, Makoto Hara, Hideto Nakajima
Division of Neurology, Department of Medicine, Nihon University School of Medicine, Tokyo, Japan

Background: A concept of sensory tracts in the spinal cord has been established in relation to a dorsolateral pathway which is located in the posterior part of the lateral column and conveys the deep sense.

Methods: The clinical status at onset, neurological symptoms, and magnetic resonance imaging (MRI) findings in 13 patients of spinal cord infarction were studied.

Results: The clinical status was acute in 11 patients and subacute in 2 patients. Ischemia spread bilaterally in 12 patients; lateral involvement was noted in 1 patient. Palsy of the extremities was noted in 11 patients. Segmental sensory disturbance was shown in all patients. One patient showed disturbance of all senses and paraplegia, which indicated transverse myelopathy. In the other 12 patients, 11 patients showed impairment of pain sense although joint position sense was preserved, excluding 1 patient whose sensory disturbance showed dysesthesia alone. In these 11 patients, soft touch and vibration senses were impaired in 7 patients. Abnormality of spinal cord MRI was detected in 7 patients. The lesions were located in the cervical cord in 3 patients, cervical to thoracic cord in 1 patient, and thoracic cord in 3 patients.

Discussion: In the 11 patients in whom pain sense was impaired and joint position sense was preserved, involvement of the anterior spinal cord artery (ASCA) was the mainstay. Impairment of vibration sense was accompanied in 7 patients in patients of ASCA infarction. It was speculated that impairment of vibration sense can occur in patients with ASCA infarction whose ischemia spread to the dorsolateral pathway in the posterior part of the lateral column. Additionally, preservation of joint position sense in these 7 patients indicated that a large proportion of the neurofibers for joint position sense are considered to be localized in the posterior column.
On-demand oral presentation

O-17 The usefulness of the 3D-Allcock test in evaluating the origin of tubelothalamic artery

Yusuke Takahashi, Hiroaki Shimizu
Department of Neurosurgery, Akita University Graduate School of Medicine, Akita, Japan

Background: The tuberothalamic artery (TTA) is a perforating branch of the posterior communicating artery (pcom). The TTA branches from the posterior communicating artery to the anterior thalamic nucleus group. The TTA sometimes branches immediately after the posterior communicating artery branches from the internal carotid artery. In large aneurysms, the TTA may origin from aneurysm body and cause a thalamic infarction after embolization. We report a case in which the 3D-Allcock test was useful in a patient who had difficulty in determining whether the TTA branched directly from the aneurysm or from the posterior communicating artery.

Case: 73-year-old woman. A left internal carotid artery aneurysm was discovered incidentally during a preoperative examination for valvular disease. Allcock test revealed the TTA, but the origin of the TTA could not be evaluated. Under general anesthesia, the internal carotid artery was blocked with a balloon, the patient was placed in respiratory arrest, and 3D-DSA was performed from the vertebral artery. The 3D-Allcock test confirmed that the TTA was branching from the posterior communicating artery, and coil embolization was then performed safely. 3D-DSA from the vertebral artery after embolization revealed TTA and no infarction in the thalamic perforating branch region.

Conclusion: We experienced a case in which detailed cerebral angiography allowed us to evaluate the TTA's run and treat it safely.
Objective: Evaluation of cerebrovascular reactivity (CVR) using (ACZ)-challenged single photon emission computed tomography (SPECT) is accepted as a useful tool in predicting the occurrence of hyperperfusion after carotid endarterectomy (CEA). However, SPECT has disadvantages including a limited availability and long scan time. We investigated whether a measurement of neuroparenchymal blood volume (PBV), which available from data of angiography, can be alternative tool of the CVR on SPECT.

Methods: Thirty-four patients with unilateral carotid artery steno-occlusive disease were enrolled from April 2018 to August 2021, and the severity of hemodynamic compromise was assessed by Neuro PBV system (syngo Neuro PBV IR, Siemens Medical Solutions, Erlangen, Germany) and acetazolamide-challenged SPECT of the brain. Cerebral blood volume (CBV) was measured using a C-arm flat detector angiographic system. The asymmetry ratio (AR) of CBV in the middle cerebral artery (MCA) territory (CBV_{AR}) was defined as the (CBV on the lesion side / CBV on the contralateral side) × 100 (%). Cerebral blood flow (CBF) was quantified by SPECT using the quantitative SPECT/dual-table autoradiography method. Cerebrovascular reserve (CVR) in the MCA territory was defined as (CBF after ACZ challenge – CBF at rest) / CBF at rest × 100 (%) and classified as reduced (<18.4%) or non-reduced (≥18.4%).

Results: Nine patients showed reduced CVR. The CBV_{AR} was significantly lower in the reduced CVR group than in the non-reduced CVR group (84.41% vs. 99.10%, p = 0.001). The cut-off value of CBV_{AR} for predicting reduced CVR obtained from analysis of the receiver operating characteristic curve was 89.59% (sensitivity 77.8% and specificity 80.0%), and the area under the curve was 0.85 (95% CI: 0.704–0.994).

Conclusion: Our small study revealed good correlation between CBV_{AR} measured using the Neuro PBV system and CVR assessed by SPECT.
On-demand oral presentation

O-19 The differentiative finding between central and peripheral vertigo

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Background: Central vertigo is sometimes difficult to distinguish from peripheral vertigo in the emergency setting. We examined the findings that distinguish central vertigo from peripheral vertigo and assessed their clinical utility.

Methods: We conducted retrospective analysis of patients who required urgent hospitalization by vertigo in our hospital from January 2019 to December 2019. To distinguish central and peripheral vertigo, we took brain MRI or CT in all patients with vertigo at emergency room. Central vertigo was defined as acute ischemic or hemorrhagic stroke. We compared the clinical and imaging findings between central and peripheral vertigo. Sensitivity, specificity, and likelihood ratio (LR) of each clinical and imaging finding were also calculated.

Results: Of all 289 patients who visited our hospital with vertigo, 123 patients (43 male, age 71 interquartile range [IQR, 55-77]) were enrolled as available cohort. Brain MRI were performed in 108 patients (88%) and the rest undergo brain CT. Central vertigo was present in 27 patients (22%). On univariate analysis, some neurological symptoms other than vertigo (72% vs. 4%, p<0.01), low density area in brain CT (37% vs. 5%, p<0.01) and high intensity area of diffusion weighted imaging (DWI) in MRI findings (96% vs. 5%, p<0.01) were observed in central vertigo. Any neurological symptoms other than vertigo (sensitivity 69%, specificity 83%, positive LR 20.3, negative LR 0.05) and DWI findings (sensitivity 96%, specificity 95%, positive LR 19.2, negative LR 0.04) had high discriminative performance for central vertigo.

Conclusions: About one fifth of patients with vertigo who need urgent hospitalization were central vertigo. The presence of any neurological symptoms other than vertigo and MRI are useful to avoid misdiagnosis of central vertigo.
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On-demand oral presentation

O-21  Hidden bow hunter’s syndrome diagnosed with dynamic digital angiography and successfully treated with spine surgery: a case report

Satoshi Miyamoto\textsuperscript{1,3}, Mikito Hayakawa\textsuperscript{2,3}, Sho Okune\textsuperscript{3}, Takato Hiramine\textsuperscript{3}, Akinari Yamano\textsuperscript{1,3}, Toshihide Takahashi\textsuperscript{1,3}, Hisayuki Hosoo\textsuperscript{1,3}, Yoshiro Ito\textsuperscript{1,3}, Aiki Marushima\textsuperscript{1,3}, Masao Koda\textsuperscript{4}, Eiichi Ishikawa\textsuperscript{1}, Yuji Matsumaru\textsuperscript{1,2,3}

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Background
Bow hunter’s syndrome (BHS) is a rare stroke subtype caused by neck rotation or extension-induced reversible vertebral artery (VA) occlusion. Hidden BHS (HBHS) is an even rarer subtype of BHS in which an occluded VA at neutral neck position gets recanalized and causes embolic stroke at a certain neck position. Same as BHS, soft tissues, osteophytes or tumors are the main causes of unilateral VA compression in HBHS. However, because the culprit VA is occluded in neutral neck position, making this diagnosis is quite difficult. Here, we report a case of 69-year-old man who had repeated posterior circulation embolisms and diagnosed with HBHS.

Case
A 69-year-old man was admitted to our hospital complaining of sudden dizziness and dysarthria. He had left-sided sensory loss, right homonymous superior quadrantanopia. MRI showed posterior circulation infarctions with the right VA occlusion. Diagnosed as an atherothrombotic brain infarction, antiplatelets therapy started. However, 4 months later, he repeated embolic stroke in the posterior circulation territory. Digital angiography showed the right VA was occluded in neutral neck position but got recanalized with left lateral flexion of his neck; led us to the diagnosis of HBHS. Osteophytes and soft tissues compressed his right VA at C6 level on MRI, then we conducted decompression of the VA. Right VA remained open in any neck position after the surgery and no recurrence of infarctions were seen.

Conclusion
We experienced a case of HBHS in which occluded right VA in neutral position got recanalized with contralateral lateral flexion of neck and caused repeated posterior circulation embolisms. HBHS can be missed easily but it’s important to diagnose HBHS correctly because it’s a reversible disease by a surgical treatment as in this case.

When we see repeated posterior circulation infarctions with unilateral VA occlusion, we should consider the possibility of HBHC.
Background: The left atrium (LA) is one of the primary locations for the thrombus formation that causes an ischemic stroke. We aimed to evaluate whether left atrial function parameters, including left atrial strain, are associated with ischemic stroke subtypes.

Methods: We retrospectively included acute ischemic patients who underwent transthoracic echocardiography. Left atrial strain is assessed by 2-dimensional speckle tracking echocardiography. Stroke etiology was classified into cardioembolic, non-cardioembolic stroke, or embolic stroke of undetermined source (ESUS). Cardioembolic stroke only included stroke with high-risk cardioembolic sources. Univariate and multivariable logistic regression analyses were conducted to assess the associations between left atrial function and stroke etiologies.

Results: A total of 242 patients with acute ischemic stroke were classified into cardioembolic sources (n=43), non-cardioembolic stroke (n=142), and ESUS (n=57). LA diameter and left atrial volume index (LA VI) were higher in cardioembolic stroke. Left atrial reservoir, conduit, and contractile strain were significantly low in cardioembolic stroke. Multivariable analyses showed an independent association between cardioembolic stroke and LA diameter (OR, 1.122; 95% CI, 1.042-1.207), LA VI (OR, 1.107; 95% CI, 1.064-1.151), mitral E/A ratio (OR, 8.072; 95% CI, 1.865-34.942), LA reservoir strain (OR, 0.798; 95% CI, 0.739-0.862), LA conduit strain (OR, 0.898; 95% CI, 0.826-0.975), LA contractile strain (OR, 0.739; 95% CI, 0.666-0.821), and left ventricular EF (OR, 0.887; 95% CI, 0.837-0.939). However, echocardiographic parameters were not independently associated with ESUS.

Conclusions: Our study demonstrated that left atrial functions assessed by strain analyses were independently associated with cardioembolic stroke. On the other hand, the fraction of ESUS with hidden cardioembolic sources is presumed to be low considering no association between LA function and ESUS.
Background and aims: Cerebral vasospasm is one of the serious complications affecting poor outcome after aneurysmal subarachnoid hemorrhage (SAH). Although several reports have proved the association of SAH volume or intraventricular hematoma (IVH) with vasospasm, there is no classification based on SAH distribution. In this study, we aimed to propose simple classification on computed tomography (CT) to predict symptomatic vasospasm (SVS).

Methods: We performed a single center retrospective study from January 2010 to April 2020. All SAH patients who CT scan was performed within 24 hours of symptom onset were included. We analyzed the SAH distribution, IVH, massive IVH, intraparenchymal hematoma, sylvian hematoma, and subdural hematoma. The SAH distribution was classified in three groups according to our unique definition as bellows; Group A: SAH localized in basal cistern and posterior fossa, Group B: SAH localized around the circle of Willis, and Group C: diffuse SAH spread to the convexity cortical sulcus. Odds ratios for SVS were calculated for SAH distribution and each finding of the CT scan. All predictive factors were analyzed with multiple logistic regression.

Results: A total of 264 patients were included in this study and 44 patients developed SVS. Among the CT findings we investigated, group C was the most affective predictor of SVS (OR 10.1, 95 CI 1.28 to 79.3). IVH, ICH, sylvian hematoma, and massive IVH were not related to the development of SVS in this analysis.

Conclusions: We developed a simple CT classification to predict SVS based on initial SAH distribution. Our unique and new CT classification can provide useful clues for the prediction of SVS in patients with SAH.
**Background and Purpose:** Balloon occlusion test (BOT) is performed to evaluate ischemic tolerance before the treatment of giant cerebral aneurysms, neck tumors or skull base tumors that may require parent artery occlusion. Single-photon emission computed tomography (SPECT) is the most common modality to evaluate cerebral blood flow during BOT, however, using SPECT has some problems including patient transportation and handling and management of radioisotopes. The purpose of the current study was to compare RAPID for Angio to SPECT as an alternative technique during BOT.

**Methods:** Thirteen consecutive patients who underwent BOT from June 2021 and June 2022 were included in this study. BOT procedures were performed with SIEMENS ARTIS icono D-Spin. 5.2Fr Selecon MP catheter II (Terumo) was placed into the internal carotid artery on the affected side and balloon occlusion was performed. The presence of neurological symptoms, mean blood pressure, mean stump pressure, and rSO2 are measured for 15 minutes. If neurologically tolerant, RAPID is performed at 7.5 minutes after the start of BOT, and the balloon is deflated after 15 minutes. The patient is then moved to the SPECT room, the balloon is inflated again, and SPECT study using 99mTc-HMPAO is performed.

**Results:** Thirteen patients included 9 patients with unruptured aneurysms, 1 patient with common carotid artery dissection, 1 patient with neck tumor, 1 patient with pituitary apoplexy, and 1 patient with direct CCF. The mean age was 61.8 years, and 11 patients were neurologically tolerant. In total, eight patients were analyzed for which both RAPID for ANGIO and SPECT results were available, and Tmax showed the best correlation with SPECT’s CBF. The second correlated was MTT, while no correlation was observed for CBV and CBF.

**Conclusion:** Tmax of Rapid for Angio nicely reflects CBF in SPECT-RAPID is useful as an alternative technique instead of SPECT in BOT.
On-demand oral presentation

O-25 The clinical significance of calcification in vulnerable carotid plaque

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Purpose: Calcification pathogenesis and the relationship between calcification and plaque composition remain unclear. This study explored the calcification characteristics of vulnerable plaques, especially focusing on calcification thickness, using computed tomography and magnetic resonance plaque imaging.

Methods: Demographic, CTA, and MR plaque imaging data were acquired from 178 patients with 229 lesions diagnosed with carotid stenosis. The calcification types were categorized by calcification thickness. We evaluated their features, including the anatomical location and the plaque composition compared with MR plaque imaging, and clarify the clinical characteristics. Furthermore, an immunohistochemical subgroup analysis was performed on 84 lesions treated with carotid endarterectomy.

Results: The result of the ROC analysis suggested the threshold between symptomatic and asymptomatic calcification was 2.04 mm (AUC:0.841, 95%CI: 0.771-0.894). Calcification with ≥ 2 mm thickness was classified as thick calcification and < 2 mm thickness as thin calcification. Multivariate analysis suggested the prevalence of symptomatic patients in the thin calcification group was significantly higher than others (P = 0.01; odds ratio, 4.1; 95% confidence interval 2.8-7.2). Plaques with thin calcification were associated with plaque with intraplaque hemorrhage (P < 0.01). The interobserver reliability (κ) of calcification type was 0.962 (95% confidence interval, 0.941-0.988). Immunohistochemical analysis demonstrated that the numbers of CD68-positive cells and CD31-positive microvessels in shoulder lesions were significantly higher in the thin calcification group than in the non-thin group (both P < 0.01).

Conclusions: Thin calcification was associated with plaques with intraplaque hemorrhage and had different clinical implications than thick calcification.
On-demand oral presentation

**O-26 Thalamostriate vein dilatation and brush sign on susceptibility-weighted imaging as predictors of progressing stroke**

Shota Yoshimura¹, Yoichi Morofuji¹, Ayaka Matsuo¹, Eri Shiozaki¹, Genki Chikamatsu¹, Yuka Ogawa¹, Hikaru Nakamura², Kazuaki Okamura¹, Ryotarou Takahira¹, Susumu Yamaguchi³, Shirou Baba¹, Kenta Ujifuku¹, Takeshi Hiu¹, Kouichi Yoshida¹, Yukishige Hayashi², Tsuyoshi Izumo¹, Yoshiharu Tokunaga⁴, Takayuki Matsuo¹

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**Background**

Branch atheromatous disease (BAD) in the lenticulostriate artery area is strongly associated with early neurological deterioration. Recent reports indicate that susceptibility-weighted imaging (SWI) is one of the surrogate marker for penumbra in large vessel occlusion.

In this study, we investigated whether the finding of thalamostriate vein (TSV) dilatation or brush sign (BS) on SWI in the LSA region can predict infarct growth and neurological deterioration.

**Methods**

We performed a single center retrospective study from April 2018 to March 2020. We included patients with cerebral infarction in the LSA region who presented within 24 hours of onset. MRI including SWI was performed on admission and within 1 week after admission. TSV dilatation was defined as the difference in the diameter of the TSV between the right and left sides on SWI on admission. The volume ratio of the hyperintense area on diffusion-weighted imaging (DWI) between on admission and follow up was measured. cerebral infarct growth rate was calculated. Worsening of paralysis was defined as a manual muscle test (MMT) 1 or higher.

**Results**

A total of 358 patients were included in this study and 13 patients were presented with TSV dilatation or BS. Patients with TSV dilatation or BS showed significantly enlarged cerebral infarcts (p=0.0026) and worsened paralysis (p<.0001). TSV dilatation or BS was associated with cerebral infarct size (>15 mm in diameter) in axial section (p=0.012), but not with the size in coronal section (p=0.53). Other factors including patient’s back ground, treatment method were not associated with cerebral infarct size or worsening paralysis.

**Conclusion**

In cerebral infarction in the LSA region, the presence of TV dilatation or BS is a predictor for cerebral infarct growth and worsening paralysis.
On-demand oral presentation

**0-27 Clinical significance of small ischemic lesions accompanied with intracerebral hemorrhage**

Motohiro Okumura, Takeo Sato
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**Background and Purpose:** Small ischemic lesions (SILs) are sometimes accompanied with intracerebral hemorrhage (ICH), but the clinical significance of SILs on ICH remains unclear. Some polyunsaturated fatty acids (PUFAs) are related to the incidence of stroke. We aimed to determine the influence of SILs on prognosis and the association between serum PUFAs and the development of SILs.

**Methods:** Consecutive patients with ICH who underwent MRI and measured PUFAs within 7 days from admission were included. We also evaluated the following cerebral small vessel disease markers detected on MRI; severe white matter hyperintensity scale defined as greater than 2 (separately scored by periventricular hyperintensity and deep and subcortical white matter hyperintensity), the presence of cerebral microbleeds, and old lacunes. An unfavorable outcome was defined as a modified Rankin Scale score of 3 to 6 at 3 months from onset. We assessed whether SILs could be associated with unfavorable outcomes and whether some PUFAs levels could be the factors associated with SILs.

**Results:** We screened 377 consecutive patients with ICH, including 272 patients (180 [66%] male, median age 62 years). Of 272 patients, SILs coexisted in 38 (14%) patients and 102 (38%) patients had unfavorable outcomes. In multivariable logistic regression analysis, SILs were independently associated with unfavorable outcomes (odds ratio [OR] 2.638, 95% confidence interval [CI] 1.007-6.909, \( p = 0.048 \)). In addition, the factors associated with SILs were docosahexaenoic acid (DHA) / arachidonic acid (AA) ratio (OR 0.172, 95% CI 0.040-0.736, \( p = 0.018 \), Figure) and old lacunes (OR 3.374, 95% CI 1.074-10.599, \( p = 0.037 \)).

**Conclusions:** Small ischemic lesions might be related to unfavorable outcomes after ICH and a lower level of DHA/AA ratio might be associated with the development of SILs.

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<thead>
<tr>
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<th>Crude OR (95% CI)</th>
<th>( p )</th>
<th>Multivariate OR (95% CI)</th>
<th>( p )</th>
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<tr>
<td>Severe periventricular hyperintensity</td>
<td>2.281 (1.099-4.735)</td>
<td>0.027</td>
<td>1.680 (0.757-3.726)</td>
<td>0.202</td>
</tr>
<tr>
<td>Microbleeds</td>
<td>4.763 (1.421-16.093)</td>
<td>0.011</td>
<td>2.344 (0.633-8.683)</td>
<td>0.202</td>
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<tr>
<td>Old lacunes</td>
<td>4.703 (1.613-13.714)</td>
<td>0.005</td>
<td>3.374 (1.074-10.599)</td>
<td>0.037</td>
</tr>
<tr>
<td>Docosahexaenoic acid / arachidonic acid</td>
<td>0.212 (0.054-0.832)</td>
<td>0.026</td>
<td>0.172 (0.040-0.736)</td>
<td>0.018</td>
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Logistic regression analysis for factors associated with small ischemic lesions in ICH patients.

Adjusted OR (95% CI)

- Without small ischemia lesions
- With small ischemia lesions
On-demand oral presentation

0-28 Stroke mimics diagnosed with disorder of cervical spine and cord

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Department of Neurosurgery, Seirei Memorial Hospital, Ibaraki, Japan

For disorder of cervical spine and cord, some cases present with impaired consciousness and preceding acute onset hemiplegia. In such cases, we consider stroke as a differential diagnosis. In cases of progressive symptoms, a definitive diagnosis may be difficult to reach partly on account of time constraints before treatment. Since our institution treats spinal disease, we often encounter patients with stroke mimics later diagnosed with disorder of cervical spine and cord. The disorders include various types such as hemorrhage, neoplasia, trauma with unclear episodes, and so on. Accordingly, the treatment also varies widely. We report such cases while giving concrete examples.
Introduction
The association between cancer and stroke has been continuously reported. The mechanism of cancer related strokes is intravascular coagulation, and others can cause strokes due to non-bacterial thrombotic endocarditis, deep vein thrombosis, and cerebral venous thrombosis. In ischemic stroke patients with cancer, the prognosis may be worse than stroke without cancer, evaluation of etiology is important for treatment, management and clinical outcome.

Case
A 57-year-old man came to the emergency room with paresthesia and weakness of left-hand that occurred three hours ago. Three months ago, he was taking anticoagulants for thrombosis in the right brachiocephalic vein. The body temperature was 36.5°C, chest X-ray, and electrocardiogram were normal. Hemoglobin, leukocytes, C-reactive protein and erythrocyte sedimentation rate were normal. In the blood clotting test, it was elevated to D-dimer 2439ng/mL, but PT, INT were normal range. Diffusion weighted image of brain magnetic resonance imaging showed multiple ischemic lesions in both middle cerebral artery territories(Figure A). Brain magnetic resonance angiography was no significant stenosis(Figure B). Trans-thoracic echocardiography found a mass of 0.44*0.45cm in the mitral valve(Figure C). But no bacteria have been identified in the blood culture. On the second week, edema and venous congestion in the left lower clavicle and arm(Figure D). Upper limb angiography computed tomography confirmed thrombosis of the left brachiocephalic vein(Figure E). Small nodules were palpated in the left lower clavicle area, and immunochemistry and biopsy were performed(Figure F). Metastatic pulmonary adenocarcinoma was diagnosed based on biopsy and positive results of CEA, Napsin-A, and PD-L1.

Conclusion
In stroke patient accompanied by cancer related thrombosis such as non-bacterial thrombotic endocarditis and upper extremity deep vein thrombosis, metastatic pulmonary adenocarcinoma diagnosed to confirm the association between cancer and stroke. It emphasizes the importance of evaluating the etiology and cause of rare thrombosis.
On-demand oral presentation

0-30  The impact of patency of internal carotid artery terminus on the early clinical outcome in patients with acute internal carotid artery occlusion and mild symptoms

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Introduction: Both collateral flow via internal carotid artery (ICA) terminus and initial mild symptoms might be associated with favorable outcome in patients with acute ICA occlusion (ICAO). The present study aimed to address the association between the early clinical outcome and the patency of ICA terminus in patients of acute ICAO with mild symptoms.

Methods: Of 1214 consecutive patients with acute ischemic stroke or transient ischemic attack due to large vessel occlusion, patients with ipsilateral ICAO and initial National Institutes of Health Stroke Scale score (NIHSS) ≤ 5 were retrospectively enrolled. We examined the association between clinical factors including patency of ICA terminus and recurrence of stroke or early neurological deterioration with increment in NIHSS score ≥ 1 during hospital stay (REND).

Results: Thirteen of 35 patients who were finally enrolled had REND (37 %), and median mRS at discharge was 1 [interquartile range 0-4]. Initial NIHSS score (4 vs. 1, p<0.001), the rate of diabetes mellitus (61.5% vs 13.6%, p=0.007), intravenous thrombolysis (IVT) (30.9% vs. 0%, p=0.014), and mechanical thrombectomy (MT) (23.1% vs. 0%, p=0.044) was significantly higher in patients with REND rather than in those without. The rate of patent ICA terminus was comparable between these groups. Except for one patient who underwent MT promptly after IVT, 3 patients initially treated with IVT deteriorated after IVT. One patient without patent ICA terminus was not indicated for MT. In other 2 patients with patent ICA terminus, MT was not initially, but eventually performed because of REND due to thrombus migration, and discharged with modified Rankin Scale of 5.

Conclusion: Overall outcome of patients of acute ICAO with mild symptoms was favorable, but immediate MT as well as IVT might be reasonable as acute reperfusion therapy to prevent thrombus migration irrespective of patency of ICA terminus.

75 years old male. He was initially treated with IVT alone 200 minutes after the onset. A) DWI showed acute infarct on the left precentral gyrus on the territory of the MCA (white arrow). B) MRA showed carotid occlusion. MT was withheld because of mild symptoms (NIHSS 4) and patent ICA terminus. Five hours after the IVT, his left visual acuity had become blind which suggested the left ophthalmic artery occlusion due to thrombus migration. Five hours and 45 minutes after the IVT, he presented with global aphasia and right hemiplegia (NIHSS score 19). C) Although emergent DSA initially showed occlusion of the intracranial ICA, subsequent imaging revealed occlusion of the left distal MT MCA segment (white arrowhead). Immediate MT with MERCI retriever was performed, but significant recanalization was not obtained. D) After the MT, territorial large infarct on the MCA territory was confirmed. He was finally diagnosed as embolic stroke of undetermined source.
O-31  Apparent diffusion coefficient level is related to diffusion-weighted imaging reversal in mechanical thrombectomy patients: a retrospective cohort study

Takeru Umemura, Taketo Hatano, Takenori Ogura, Takeshi Miyata, Yuji Agawa, Hiroaki Nakajima, Hiroki Sakamoto, Yusuke Nakazawa, Koji Shiomi, Noriyuki Koga, Takashi Nagahori, Izumi Nagata

Department of Neurosurgery, Kokura Memorial Hospital, Kitakyushu, Japan

Background and Purpose: In patients with ischemic stroke, DWI lesions can occasionally be reversed by reperfusion therapy. This study aimed to ascertain the relationship between ADC levels and DWI reversal in patients with acute ischemic stroke who underwent recanalization treatment.

Materials and Methods: We conducted a retrospective cohort study in patients with acute ischemic stroke who underwent endovascular mechanical thrombectomy with successful recanalization between April 2017 and March 2021. DWI reversal was assessed through follow-up MRI approximately 24 h after treatment.

Results: In total, 118 patients were included. DWI reversal was confirmed in 42 patients. The ADC level in patients with reversal was significantly higher than that in patients without reversal. Eighty-three percent of patients with DWI reversal areas had mean ADC levels ≥ 520 × 10^{-6} mm²/s, and 71% of patients without DWI reversal areas had mean ADC levels < 520 × 10^{-6} mm²/s. The mean ADC threshold was 520 × 10^{-6} mm²/s with sensitivity and specificity of 71% and 83%, respectively. In multivariate analysis, the mean ADC level (OR, 1.023; 95% CI, 1.013–1.033, P<.0001) was independently associated with DWI reversal. Patients with DWI reversal areas had earlier neurological improvement (NIHSS at 7d) than patients without reversal areas (p<.0001).

Conclusions: In acute ischemic stroke, the ADC value is independently associated with DWI reversal. Lesions with mean ADC ≥ 520 × 10^{-6} mm²/s are salvageable by mechanical thrombectomy, and DWI reversal areas regain neurological function. The ADC value is easily assessed and is a useful tool to predict viable lesions.

This study was published in AJNR May 2022
**Background and Purpose:** Conjugate eye deviation (CED) on CT of acute ischemic stroke has been associated with large vessel occlusion (LVO), higher National Institutes of Health Stroke Scale (NIHSS) score, larger anterior circulation infarct, and worse outcomes, but has never been evaluated by CT immediately after mechanical thrombectomy (MT). The aim of the present study was to identify the frequency and prognostic value of CED immediately after MT.

**Methods:** Subjects were 51 acute stroke patients who underwent mechanical thrombectomy for anterior circulation LVO in our hospital. CED and Alberta Stroke Program Early CT Score (ASPECTS) was evaluated by CT before and after MT. Clinical data were retrospectively collected from medical records. Logistic regression was performed to determine the prognostic value of CED after MT.

**Results:** Among 51 patients, 27 (53%) had CED after MT. There was no significant difference in clinical data, including age, sex, ASPECTS, NIHSS score, occlusion vessel, alteplase use, right-sided lesion, successful recanalization, and ASPECTS after MT, regardless of the presence of CED. Significant predictors for a good outcome (modified Rankin Scale 0-2 at discharge) were younger age (<75) (Odds ratio [OR], 9.66; 95% confidence interval [CI], 1.96-70.1), lower NIHSS score (<18) (OR, 4.37; 95% CI, 1.01-24.7), successful recanalization (OR, 11; 95% CI, 2.06-87.2), and no CED after MT (OR, 7.89; 95% CI, 1.65-5.3).

**Conclusion:** CED immediately after MT is independent predictor of functional outcome in acute ischemic stroke. Immediately after MT, due to confusion or the use of sedatives, it is still difficult to estimate the final infarction volume and assess neurological deficits. The presence of CED helps to estimate the prognosis immediately after treatment.
On-demand oral presentation

**O-33 Effect of the introduction of MRI first stroke diagnosis on acute reperfusion therapy in our hospital**

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²Department of Endovascular Neurosurgery, Saitama Medical University International Medical Center, Saitama, Japan

**Introduction**

November 12, 2019, onwards, we changed the diagnostic imaging of acute cerebral infarction from performing computed tomography (CT) initially, i.e., "CT first," followed by magnetic resonance imaging (MRI), to "MRI first," which uses only MRI. We retrospectively evaluated the time for intervention and functional outcome associated with this change in patients undergoing acute reperfusion therapy (intravenous thrombolysis with rt-PA/mechanical thrombectomy).

**Method**

The MRI first data of 149 consecutive hospitalized patients with modified Rankin scale (mRS) 0–1 who underwent acute reperfusion therapy in our hospital between January 1, 2019 and December 31, 2020 was reviewed. These patients were divided into two groups: CT first (CT group: n=78) and MRI first (MRI group: n=71). Background factors were age, sex, comorbidities, smoking history, stroke types, National Institutes of Health Stroke Scale score at visit, Alberta Stroke Program Early CT Score (10-point method), % of cerebral large vessel occlusion (LVO), door-to-needle (DTN), door-to-puncture (DTP), door-to-recanalization (DTR) time (min), % of mRS 0–1 after 3 months, and symptomatic intracranial hemorrhage (sICH) were compared between the two groups.

**Result**

No significant difference was found in background factors between the two groups. DTN, DTP, and DTR average time were significantly shorter in the MRI group than in the CT group (DTN 57.4 vs. 71.4 [P = 0.005], DTP 53.2 vs 81.5 [P < 0.001], DTR 129.8 vs 171.4 [P = 0.001]). mRS 0-1 (%) was not different between the two groups (31 vs. 29 [P = 0.860]), and sICH (%) were not significant but lower in the MRI group (1.6% vs. 6.4% [P = 0.212]).

**Conclusion**

Although the change to MRI first significantly reduced DTN, DTP, and DTR times, functional outcomes did not alter.
On-demand oral presentation

**0-34  Hemorrhagic complications of mechanical thrombectomy: associated factors and their managements**

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³Department of Endovascular Neurosurgery, Saitama Medical University, International Medical Center, Saitama, Japan

**Introduction:** Mechanical thrombectomy (MT) is an effective treatment, but MT carries the risk of hemorrhagic complications (HC). In this study, we analyzed the associated factors of HC, and reviewed underlying pathophysiology, and strategies for early recognition and treatment.

**Materials and Methods:** HC were retrospectively collected experienced at Saitama Medical University International Medical Center and related facilities from April 2017 to March 2022. Three hundred and twelve patients underwent mechanical thrombectomy, 193 males and 119 females, (mean age: 75.2 years). These included 209 cases with cardiogenic embolizations, 78 cases were atherothrombosis, and 17 other cases. The occlusion sites were internal carotid artery (ICA) in 84 cases (26%), proximal M1 in 58 cases (18%), distal M1 in 86 cases (27%), M2: 45 cases (14%), basilar artery (BA) in 25 cases (8%). Related factors were examined in relation to HC.

**Results:** The HC group consisted of 38 cases (14.5%). The mean age was 77.9 years, older than that of the uncomplicated (non-HC) group (74.8 years), without significant (p=0.063). No significant association was found except the TICI score showed a large number of TICI 2B in the HC group and TICI 3 in the non-HC (chi-square test p<0.001). Complications by site of occlusion, the frequency of M2 was slightly higher without significant (p=0.79). Among 38 patients, 24 (63.1%) were related to intraoperative procedures. There were 6 fatal cases. Five cases were considered to be procedure-related, and one of them was associated with postoperative fatal cerebral hemorrhage.

**Conclusions:** These complications can be divided 1) intraprocedural bleeding, 2) postprocedural, reperfusion injury unavoidable complications. The majority of patients in the HC group experienced minor bleeding, however, some of them may cause major bleeding with poor prognosis. It was considered that the devices and procedures should be simplified, such as standardization among hospitals, and that could reduce the number of HC.
On-demand oral presentation

**O-35** Baseline NIHSS score correlates hypoperfused tissue volume based on CT perfusion processed using RAPID software

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**Background**

Difference between the hypoperfused tissue volume and the ischemic core volume indicates the penumbral tissue volume in acute stroke patients due to large vessel occlusion (LVO). Without multimodal brain imaging or automated software processing, the hypoperfused tissue volume would be presumed from the baseline National Institutes of Health Stroke Scale (NIHSS) score. However, it has not been well investigated whether the baseline NIHSS score was correlated with the volume of hypoperfused tissue, defined by Tmax >6 seconds measured using RAPID (iSchemView). The aim of this study was to clarify the relationship between the baseline NIHSS score and the Tmax >6 seconds volume.

**Methods**

We retrospectively analyzed patients with acute anterior circulation LVO who underwent non-contrast CT, CT angiography and CT perfusion with RAPID processing within 24 hours of onset between July 2019 and June 2022 in our hospital. Correlations between patients’ baseline characteristics and the Tmax >6 seconds volume were investigated.

**Results**

A total of 46 patients (mean age, 78.6 years; female, 23 patients; median baseline NIHSS score, 18.5; and 9 patients were performed multimodal CT imaging beyond 6 hours from onset) were included. The Tmax >6 second volume (median, 110 mL) increased as the baseline NIHSS score increased (p=0.51, P<0.001). In 5 patients with large artery atherosclerosis (LAA), the Tmax >6 second volumes were smaller than those in patients with other stroke subtypes (median, 58 mL vs 118 mL, P=0.025). Multiple linear regression analysis for baseline NIHSS score and LAA subtype revealed significant association between the baseline NIHSS and the Tmax >6 seconds volume (β=9.074; 95% confidence interval, 5.184—13.001; P<0.001). Predicted hypoperfused tissue volume was equal to 9.074 × (baseline NIHSS score) — 42.894 (LAA) — 15.403, with an R² of 0.35.

**Conclusions**

The baseline NIHSS score significantly correlated with the hypoperfused tissue volume measured using RAPID.
On-demand oral presentation

0-36 Factors related to white thrombi in acute ischemic stroke in cancer patients

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1Department of Neurosurgery, Kurashiki Central Hospital, Kurashiki, Japan,
2Department of Neurosurgery, Kitano Hospital, Tazuke Kofukai Medical Research Institute, Osaka, Japan,
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Objectives: Thrombi in cerebral large vessel occlusion associated with active cancer are often fibrin and platelet-rich white thrombi. However, evaluating the thrombus composition in a short time before thrombectomy is often ineffective. We sought to determine factors related to white thrombi in acute ischemic stroke due to large vessel occlusion in cancer patients.

Methods: Consecutive cancer patients undergoing thrombectomy for acute ischemic stroke due to large vessel occlusion between January 2018 and May 2022 were retrospectively reviewed. The patients were classified into white thrombus and red thrombus groups on the basis of the pathological findings of retrieved thrombi. Patient characteristics and laboratory findings were compared between the two groups.

Results: There were 12 patients in the white thrombus group and 11 patients in the red thrombus group. Active cancer was significantly more in the white thrombus group than in the red thrombus group (91.7% vs. 36.3%, p = 0.0094). Internal carotid artery occlusion was significantly less in the white thrombus group than in the red thrombus group (0% vs. 36.4%, p = 0.037). Among laboratory findings, D-dimer levels were an independent factor associated with white thrombi (odds ratio 8.97 [95% confidence interval 1.71–368.99], p<0.0001). The cut-off value of D-dimer levels for predicting white thrombi was 3.5 μg/mL (100% sensitivity and 83.3% specificity).

Conclusions: In acute ischemic stroke due to large vessel occlusion associated in cancer patients, active cancer, no internal carotid artery occlusion, and higher D-dimer levels may be associated with occlusion with fibrin and platelet-rich white thrombi. If a white thrombus is predicted from a D-dimer level of >3.5μg/mL before thrombectomy, a procedure with contact aspiration or the combined technique may be useful for early recanalization.
Background: Mechanical thrombectomy (MT) is a time-dependent emergency procedure for patients with acute ischemic stroke (AIS). Our hospital on the mainland serves as a hub center for eight hospitals on the remote islands of Nagasaki Prefecture, Japan. We can transfer emergency patients from these islands to our hospital at any time, using a teleradiology system and helicopter transport. The aim of this study was to investigate clinical outcomes of patients with AIS in remote islands who underwent MT and compare the differences between nighttime with daytime.

Methods: During 2014-2020, we reviewed consecutive patients with AIS who received MT. Patients were divided into “daytime” group and “nighttime” group. Cases with a consultation time from islands hospitals of 7:00 to 17:00 were defined as daytime, and other hours were defined as nighttime.

Results: We included 22 patients (daytime group: 14 patients. Nighttime group: 8 patients). Daytime group was transferred by Helicopter emergency medical services (HEMS) and nighttime group was transferred by Maritime Self-Defense Force (MSDF) helicopter. Door to door time in the nighttime group (median 279 min) was longer than that in the daytime group (median 210 min) (P= 0.00196). On the other hand, there were no significant differences in mRS 0-2 at 90 days, hemorrhagic complication, and mortality.

Conclusions: Transport time in the nighttime was longer than in the daytime. However, the clinical outcomes of the nighttime group were comparable to that of daytime group. Our 24-h helicopter transportation system can provide safe MT for patients with AIS on remote islands.
### O-38 Intravenous rt-PA therapy promotes neurological improvement after effective (TICI 2b-3) mechanical thrombectomy

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**Purpose:** This study aimed to examine the factors associated with neurological improvement after TICI 2b or TICI 3 reperfusion in acute ischemic stroke (AIS) patients treated with mechanical thrombectomy (MT).

**Methods:** Of 62 consecutive patients with AIS who underwent MT since 2018 at our hospital, we analyzed 45 patients having achieved TICI 2b or TICI 3 reperfusion. Their mean age was 76 (57-90) years and 28 were male. Neurological improvement was defined as NIHSS score 0-1 at discharge or ≥10 points improvement during admission. Patients’ demographic data, ASPECTS, intravenous rt-PA therapy, MT achievement (first pass recanalization and TICI 3 recanalization), postoperative bleeding, short (<270 min) time from onset to recanalization (O2R), and other factors were examined, using multivariate analysis.

**Results:** Intravenous rt-PA was administered prior to MT in 29% of patients, recanalization at MT first pass was achieved in 60% and TICI 3 recanalization in 69% of patients. 62% of patients had recanalization with O2R < 270 min. Multivariate analysis showed that intravenous rt-PA therapy (p=0.043, OR 20.2) and ASPECTS 7 or higher (p=0.009, OR 27.1) significantly correlated with excellent neurological improvement during admission.

**Conclusions:** In patients with effective recanalization of TICI 2b or 3, pre-MT intravenous rt-PA therapy and high ASPECTS were significantly associated with excellent neurological improvement during hospitalization. The thrombolytic effect of rt-PA against micro-emboli after MT may have contributed to improve neurological symptoms in patients with effective (TICI 2b or TICI 3) MT.

### Factors related NIHSS improvement after TICI 2b or 3 reperfusion

<table>
<thead>
<tr>
<th>variable</th>
<th>NIHSS improvement (+)</th>
<th>NIHSS improvement (-)</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>30</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>age &gt;75 (n=25)</td>
<td>15 (50%)</td>
<td>10 (67%)</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>sex male (n=28)</td>
<td>19 (63%)</td>
<td>9 (60%)</td>
<td>0.82</td>
<td></td>
</tr>
<tr>
<td>LVO (n=37)</td>
<td>26 (87%)</td>
<td>11 (73%)</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>cardioembolic (n=37)</td>
<td>25 (83%)</td>
<td>12 (80%)</td>
<td>0.78</td>
<td></td>
</tr>
<tr>
<td>iv rt-PA (n=13)</td>
<td>12 (40%)</td>
<td>1 (6.7%)</td>
<td>0.33</td>
<td>20.2</td>
</tr>
<tr>
<td>first pass (n=27)</td>
<td>21 (70%)</td>
<td>6 (40%)</td>
<td>3.5</td>
<td>0.053</td>
</tr>
<tr>
<td>TICI 3 (n=31)</td>
<td>22 (73%)</td>
<td>9 (60%)</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>ASPECTS ≥7 (n=36)</td>
<td>28 (93%)</td>
<td>8 (53%)</td>
<td>12.25</td>
<td>27.1</td>
</tr>
<tr>
<td>hemorrhage (n=4)</td>
<td>1 (3.3%)</td>
<td>3 (6.7%)</td>
<td>0.13</td>
<td>0.03</td>
</tr>
<tr>
<td>O2R ≤270min (n=28)</td>
<td>19 (63%)</td>
<td>9 (60%)</td>
<td>0.82</td>
<td></td>
</tr>
</tbody>
</table>

* NIHSS of 0-1 or ≥10-point improvement at discharge
On-demand oral presentation

**O-39  Association between oral anticoagulants and stroke severity at onset in elderly patients with cardioembolic stroke due to non-valvular atrial fibrillation**

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**Background**  
This study aimed to determine whether oral anticoagulant therapy affects the severity of cerebral infarction at onset in elderly patients with non-valvular atrial fibrillation.

**Methods**  
This retrospective study included 330 elderly patients (aged ≥75 years) who were hospitalized for cardioembolic stroke due to non-valvular atrial fibrillation. Patient medical history, stroke severity (National Institutes of Health Stroke Scale score) at onset, and the prevalence of large vessel occlusion were compared between patients who had (n=109) and had not (n = 221) received oral anticoagulant therapy (IRB No. 2021-097).

**Results**  
Stroke severity was significantly lower in patients who had received anticoagulants compared to those who had not received anticoagulants (6 versus 12; P = 0.021). Patients who had not received anticoagulants exhibited a significantly higher prevalence of large vessel occlusion (52% versus 37%; P = 0.010). After resampling based on propensity score matching, both median stroke severity (7 versus 12; P = 0.046) and large vessel occlusion prevalence (36% versus 57%; P = 0.019) were significantly lower in patients who had undergone anticoagulant therapy.

**Conclusions**  
The results of this study suggest that elderly patients with non-valvular atrial fibrillation who are administered oral anticoagulant therapy before the onset of cerebral infarction, develop less severe strokes than those who are not undergoing such therapy. Thus, oral anticoagulant therapy should be actively considered in patients with non-valvular atrial fibrillation as it not only prevents cerebral embolism, but also reduces the risk of severe sequelae.
Diabetic ketoacidosis (DKA) is usually associated with severe hyperglycemia and dehydration in type 1 diabetes mellitus. However, it can occur rarely in the setting of normal glucose concentrations, known as euglycemic DKA, which was known to develop mostly in individuals with type 1 diabetes, or pregnant diabetic women. Sodium-glucose cotransporter 2 (SGLT2) inhibitors are new oral hypoglycemic drugs and have a pronounced glucose-lowering effect with a low risk of hypoglycemia. These medication also could reduces congestive heart failure and cardiovascular diseases. We present two cases with type 2 diabetes mellitus hospitalized for acute stroke, who developed empagliflozin-associated euglycemic diabetic ketoacidosis.

A 69-year-old woman with the history of type 2 diabetes mellitus (DM) who presented with left midbrain infarction during surgery for intertrochanter fracture in other hospital. On admission, she had euglycemic DKA and she had the history of medication of empagliflozin for one month. The HbA1c level was 12.1% and the ketone serum level of ketone body was over 9600 mmol/L. After stopping empagliflozin, ketone bodies decreased to less than 200 mmol/L.

The second patient, a 74-year-old woman with DM history presented with right IC infarction. Initial HbA1c was 9.9% but she did not take the medication for DM control. We tried oral medication including empagliflozin and the serum glucose level improved. However, she suffered from acute myocardiac infarction. After PCI, she had euglycemic DKA. Serum level of ketone body was over 7400 mmol/L and serum glucose level was below 220 mg/dL. After hydration and stopping empagliflozin, the laboratory findings improved.

Early recognition of this medical emergency like DKA and timely intervention can reduce the consequences of serious complication. However, this form of DKA could be missed by normal serum glucose levels. Clinical considerations to ensure safe SGLT2 inhibitor therapy should include appropriate monitoring parameters for timely diagnosis of euglycemic diabetic ketoacidosis.
Background: Early neurological deterioration (END) can occur frequently in patients with acute ischemic stroke with aggressive stroke symptoms and poor prognosis. When END occur, clinicians apply various treatments for improving END. This study aims to investigate which treatments are successful as rescue therapy when END has occurred in patients with lacunar stroke.

Methods: Lacunar stroke patients within 7 days of symptom onset with END during 72 hours were treated with therapeutic induced hypertension or anticoagulation groups. In the induced hypertension group, phenylephrine was administered intravenously and tapered off (10 mL/h) after 24 hours with neurologic stabilization or after using 4 days. In the anticoagulation group, argatroban was administered intravenously for 4 days. The primary endpoint was END recovery (decrease in NIHSS over 2 points or improved motor symptoms during the first 7 days). The secondary endpoint was the proportion of excellent functional outcomes (mRS 0–1) at 3 months. Safety outcomes included symptomatic intracranial hemorrhage/edema, myocardial infarction, and death.

Results: 79 and 68 patients were included in the pharmacological induced hypertension and anticoagulation groups, respectively. Therapeutic induced hypertension increased the END recovery (77.2% vs. 51.5%, P<0.01) and excellent functional outcome (mRS 0–1, 34.2% vs. 16.2%, P=0.04). After adjustment, induced hypertension (2.49 OR; 95% CI 1.06–5.81, P=0.04) and younger age were associated with END recovery.

Conclusions: Among lacunar stroke patients with END, therapeutic induced hypertension was safe and effective, showing excellent results in END recovery and functional independence at 3 months.
Backgrounds: Neurological worsening often occurs in patients with acute perforating artery infarction including branch atheromatous disease (BAD) against antithrombotic therapies, leading to poor functional outcome. However, effective antithrombotic therapy for these patients has not been established. The purpose of our study was to clarify antithrombotic strategies for BAD in primary stroke centers (PSCs) in Japan.

Methods: We conducted a web survey to 500 PSCs in Japan. We provided clinical information and DWI images of 3 different perforating artery infarction cases (2 cases with BAD in the lenticulostriate artery (LSA) or pontine paramedian artery (PPA) territory and 1 case with lacunar stroke in the LSA territory) and asked initial antithrombotic strategies and additional therapies at neurological worsening in each case.

Results: Response rate from PSCs was 38%. Dual antiplatelet therapy (Aspirin + Clopidogrel) was selected only in 9-22% as initial treatments, whereas combination therapy of 2 or more antiplatelets plus argatroban was initiated in 18% in LSA lacunar, in 59% in LSA-BAD and in 57% in PPA-BAD. A further antithrombotic agent was added at neurological worsening in approximately half of PSCs which selected 2 or more antiplatelet plus argatroban for BADs.

Conclusions: In a large number of PSCs in Japan, more aggressive antithrombotic therapies beyond current stroke treatment guideline are conducted especially for BAD. We need to verify the efficacy and safety of the aggressive antithrombotic therapies in the future.
On-demand oral presentation

**O-43  Coexisting of aortic arch atheroma and atrial fibrillation for short-term recurrence and poor functional outcome in acute stroke**

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²Department of Neurology, Shin-Oyama City Hospital, Oyama, Japan

**Background and purpose:** Multiple embolic sources are sometimes observed simultaneously in patients with embolic stroke. The present study investigated the effects of coexisting aortic arch atheroma (AAA) ≥ 4 mm thick and atrial fibrillation (AF) on short-term stroke recurrence and functional outcome.

**Methods:** Transesophageal echocardiography (TEE) was performed in consecutive embolic stroke patients, and 395 patients were classified into 4 groups according to the presence of AAA ≥ 4 mm thick and AF: AF - /AAA - group, AF + /AAA - group, AF - /AAA + group, and AF + /AAA + group. In accordance with these 4 groups, we evaluated stroke recurrence and all-cause death for 3 months after stroke onset, and also evaluated the 3-month functional outcome using the modified Rankin scale (mRS).

**Results:** Among the 128 AF patients, 39.1% also had AAA ≥ 4 mm thick. Of the 395 enrolled cases, the AF + /AAA + group showed the highest frequencies of stroke recurrence and all-cause death during 3 months after onset. On multivariate analysis, stroke recurrence or all-cause death during 3 months after onset was relatively more frequent in the AF + /AAA + group than in the AF + /AAA - group (OR, 2.34; 95% CI, 0.82-6.69; p = 0.11), but that was not statistically significant, and poor functional outcome (mRS score 3-6) at 3 months was significantly more frequent in the AF + /AAA + group than in the AF + /AAA - group (OR, 2.59; 95% CI, 1.08-6.24; p = 0.0339).

**Conclusions:** AAA concomitant with AF is not rare and appears associated with increased risks of stroke recurrence and poor functional outcome.
On-demand oral presentation

**O-44 Timing of direct oral anticoagulants for hemorrhagic transformation after endovascular treatment in acute ischemic stroke**

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²Department of Neurosurgery, Yamaguchi University School of Medicine, Yamaguchi, Japan

**Objectives:** The purpose of this study is to investigate the relationship between the timing of starting direct oral anticoagulants (DOACs) and subsequent clinical outcomes in patients with hemorrhagic transformation (HT) after endovascular treatment (EVT).

**Methods:** The subjects were patients with cardioembolic stroke who underwent EVT and received DOACs in our department from February 2017 to August 2021. Based on CT at 24 hours after EVT, the patients were classified using European Collaborative Acute Stroke Study criteria into three groups: no HT, hemorrhagic infarction (HI), and parenchymal hematoma (PH). Outcomes were assessed for incidence of recurrent ischemic stroke (RIS), new intracranial hemorrhage (ICH), and worsened HT associated with DOACs.

**Results:** Of 111 patients, 29 (26.1%) had HT, including 16 (14.4%) with HI and 13 (11.7%) with PH. The start of DOACs was significantly delayed in the PH group (no HT: 1.0 (1.0-3.0) days vs. HI: 3.0 (2.0-5.0) days vs. PH: 7.0 (7.0-10.0) days, P <0.01). The incidence of RIS did not differ significantly among the three groups, but tended to be higher in the PH group (no HT: 3.7% vs. HI: 6.3% vs. PH: 15.4%, p = 0.12). There were no cases of new symptomatic ICH. New asymptomatic ICH occurred in 2 cases in the no HT group. Worsened HT after initiation of DOACs did not occur in the HI or PH group.

**Conclusions:** The timing of starting DOACs in patients with HT after EVT may be divided by subtypes of HI and PH. In patients with HI, early initiation of DOACs can prevent RIS and is unlikely to cause new ICH or worsened HI. In PH, initiation of DOACs within 14 days appears to be safe and does not exacerbate PH. The later the start of DOACs, the higher the frequency of RIS, so early initiation of DOACs is desirable.
On-demand oral presentation

0-45 In-hospital mortality in atrial fibrillation-associated acute ischemic stroke of the intensive care unit

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3Department of Neurology, Icheon Medical Center, Icheon-si, Korea

Background
Although atrial fibrillation (AF)-associated acute ischemic stroke (AIS) is increasing, devastating, and life-threatening, data on in-hospital mortality of patients treated in the intensive care unit (ICU) is scarce. This study aimed to describe clinical course and factors associated with in-hospital mortality in AF-associated AIS in the ICU.

Methods
This study was a retrospective analysis of a prospective nationwide multicenter cohort including non-valvular AF-AIS patients admitted to 14 stroke centers in South Korea from October 2017 to March 2020. We compared the baseline characteristics between those with and without ICU care. In-hospital outcomes including early neurologic deterioration (END) and in-hospital mortality as well as rates of anticoagulation during the hospital stay were described amongst patients had ICU care. We further compared characteristics of patients resulted in in-hospital mortality and those did not. Clinical parameters associated with in-hospital mortality were analyzed using logistic regression model in ICU-treated patients.

Result
Amongst 2,487 AF-associated AIS patients included, 259 (10.4%) were treated in the ICU. Patients with ICU care were more likely to include heart failure (13.5% vs. 8.2%), while including lower prior antiplatelet (25.5% vs. 31.5%) and anticoagulant (18.9% vs. 25.5%) uses. END and in-hospital mortality were occurred in 17.0% and 7.3%, respectively. Starting anticoagulation during the hospital stay was lower in those with ICU care than did not (25.9% vs. 52.1%). Age (adjusted OR 1.09 [95% CI 1.00-1.20]), initial NIHSS score (1.29 [0.68-2.44]), platelet count (0.98 [0.97-0.995]), and END (11.29 [0.30-42.19]) were associated with the risk of in-hospital mortality.

Conclusion
ICU care in AF-associated AIS is not uncommon and establishment of treatment strategies for AF-associated AIS to reduce in-hospital mortality treated in the ICU may be needed.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Crude OR (95% CI)</th>
<th>P value</th>
<th>Model 1 OR (95% CI)</th>
<th>P value</th>
<th>Model 2 OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.07 (1.01-1.14)</td>
<td>0.014</td>
<td>1.07 (0.99-1.15)</td>
<td>0.095</td>
<td>1.09 (1.00-1.20)</td>
<td>0.049</td>
</tr>
<tr>
<td>CHA-DSc-VASc score</td>
<td>1.53 (1.04-2.25)</td>
<td>0.032</td>
<td>1.07 (0.66-1.90)</td>
<td>0.817</td>
<td>1.29 (0.68-2.44)</td>
<td>0.434</td>
</tr>
<tr>
<td>Platelet count</td>
<td>0.99 (0.98-0.999)</td>
<td>0.032</td>
<td>0.99 (0.98-0.998)</td>
<td>0.022</td>
<td>0.98 (0.97-0.995)</td>
<td>0.008</td>
</tr>
<tr>
<td>FBS</td>
<td>1.01 (1.00-1.02)</td>
<td>0.003</td>
<td>1.01 (0.99-1.02)</td>
<td>0.060</td>
<td>1.00 (0.99-1.01)</td>
<td>0.484</td>
</tr>
<tr>
<td>Initial NIHSS score</td>
<td>1.12 (1.05-1.20)</td>
<td>&lt;0.001</td>
<td>1.11 (1.03-1.21)</td>
<td>0.007</td>
<td>1.14 (1.04-1.24)</td>
<td>0.005</td>
</tr>
<tr>
<td>END</td>
<td>8.63 (3.23-23.03)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td>11.29 (3.06-42.19)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

END: early neurological deterioration, FBS: fasting blood glucose, NIHSS: National Institute for Health Stroke Scale, OR: odds ratio
*Model 1: adjusted for clinical parameters including age, CHA-DSc-VASc score, Platelet count, fasting blood sugar (FBS), and initial NIHSS score
*Model 2: adjusted for clinical parameters of model 1 and END
On-demand oral presentation

**0-46 Ischemic lesion growth in patients with a persistent target mismatch after large vessel occlusion**

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\(^2\)Department of Neurology, John Hunter Hospital, Newcastle, Australia,  
\(^3\)College of Health, Medicine, and Wellbeing, University of Newcastle, Newcastle, Australia, 
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**Background:** Failure to reperfuse a cerebral occlusion resulting in a persistent penumbral pattern has not been fully described.

**Methods:** We retrospectively reviewed patients with anterior large vessel occlusion who did not receive reperfusion, and underwent repeated perfusion imaging, with baseline imaging < 6 hours after onset and follow-up scans from 16—168 hours. A persistent target mismatch (PTM) was defined as core volume of <100 mL, mismatch ratio >1.2, and mismatch volume >10 mL on follow-up imaging. Patients were divided into PTM or non-PTM groups. Ischemic core and penumbral volumes were compared between baseline and follow-up imaging between the two groups, and collateral flow status assessed using CT perfusion collateral index.

**Results:** A total of 25 patients (14 PTM and 11 non-PTM) were enrolled in the study. Median core volumes increased slightly in the PTM group, from 22 to 36 ml. There was a much greater increase in the non-PTM group, from 57 to 190 ml. Penumbral volumes were stable in the PTM group from a median of 79 ml at baseline to 88 ml at follow-up, whereas penumbra was reduced in the non-PTM group, from 120 to 0 ml. Collateral flow status was also better in the PTM group and the median collateral index was 33% compared with 44% in the non-PTM group (p=0.043).

**Conclusion:** Multiple patients were identified with limited core growth and large penumbra (persistent target mismatch) >16 hours after stroke onset, likely due to more favorable collateral flow.
We report a case of a 92-year old female who presented with a sudden onset of right hemiparesis and neck pain mimicking ischemic stroke without trauma.

She was initially suspected to have ischemic stroke, so imaging examination of her brain was performed. MRI of the head demonstrated a DWI high signal in the left occipital lobe. In addition, MRA of the head demonstrated a severe stenosis in the left middle cerebral artery (M1). At the emergency room, however, correct diagnosis of her condition could not be determined. One day after admission, MRI of the cervical spine revealed an acute cervical epidural hematoma from the C2 to C5 levels. The epidural hematoma shifted to the left in spinal canal compressed spinal cord in axial image, which was the cause of hemiparesis and neck pain. she underwent surgical evacuation of the epidural hematoma in emergency and recovered.

Recently it has been indicated that spontaneous cervical epidural hematoma mimics ischemic stroke. Generally spontaneous cervical epidural hematoma is a rare disease and correct diagnosis is often difficult, so patients with a sudden onset of hemiparesis can be misdiagnosed as cerebral infarction even if they have neck pain. In this case, the patient was within the time window for acute ischemic stroke treatment, so it would have been possible to administer recombinant tissue plasminogen activator (rt-PA) if she had not complained of neck pain.

We should keep in mind that spontaneous cervical epidural hematoma may present as a stroke mimic, and it is very important to evaluate physical and neurological findings in detail.
On-demand oral presentation

**O-48 Stress hyperglycemia and early neurological deterioration in patients with acute LVO and low NIHSS**

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**Background and purpose:** Stress hyperglycemia has recently been used to identify the actual effect of hyperglycemia on clinical outcomes in stroke patients, but its association with collateral failure was not well defined. We investigated whether stress hyperglycemia would be associated with early neurological deterioration (END) in stroke patients with acute large vessel occlusion (LVO) who present with mild neurological deficit.

**Methods:** From a multicenter stroke registry, ischemic stroke patients with anterior circulation LVO, presented≤24 hours from the last known well, and mild symptoms at onset (NIHSS<6) were included. Endovascularly treated cases were excluded. Stress hyperglycemia ratio (SHR) was calculated as a ratio of serum glucose at arrival over glycosylated hemoglobin. END was defined as an increase in total NIHSS≥2 or any increase in the NIHSS consciousness or motor sub-scores. The effect of the SHR on END was assessed through multivariable logistic regression models.

**Results:** Among a total of 731 mild LVO patients (mean age 68.0±12.9 years; 62.7% male; 14.2% with intravenous thrombolysis), 245 (33.5%) had diabetes and 159 (21.8%) had glucose-lowering medication before the index stroke. The SHR of the patients was 22.4±6.5, which was higher in diabetic patients (21.3±5.0 vs. 25.0±8.6, p-value<0.01). END occurred in 94 (12.9%) patients. The second (T2) and third (T3) tertile groups of SHR were more likely to experience END compared to the lowest tertile group (adjusted odds ratio (aOR) 2.29 [95% confidence interval (CI), 1.26–4.17] for T2; aOR 1.85 [95% CI 1.01–3.39] for T3). The association was maintained in non-diabetic and prediabetic subgroups, but not in diabetic cases, regardless of Hb A1c levels.

**Conclusions:** Stress hyperglycemia was associated with END in acute ischemic stroke patients with mild LVO, especially in the subgroup of patients without diabetes. Non-diabetic patients with preserved physiologic response to hyperglycemia may benefit from intensive glucose control.
On-demand oral presentation

**0-49 Machine learning-based prediction of aspiration in hospitalized patients with acute stroke: efficient alternative to traditional screening tools**

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**Background:** Dysphagia and aspiration are critical complications of acute stroke, and early screening has been emphasized for an appropriate feeding strategy and nutritional management. This study aimed to establish machine learning (ML) models for screening aspiration in hospitalized patients with acute stroke.

**Methods:** This retrospective study enrolled patients with acute stroke admitted to a cerebrovascular specialty hospital between January 2016 and June 2021. Aspiration was the target outcome, and was confirmed by a videofluoroscopic swallowing study (VFSS). The Gugging Swallowing Screen (GUSS), an early assessment tool for dysphagia, was evaluated in all patients, and its predictive value was compared with that of the proposed ML models. We applied four ML algorithms to establish prediction models: regularized logistic regression (RLR), random forest (RF), extreme gradient boosting (XGB), and algorithm stacking.

**Results:** A total of 2,673 patients were included, and 392 patients presented with aspiration on VFSS. The GUSS showed an area under the receiver operating characteristics curve (AUROC) of 0.798. The RLR algorithm showed the best model among all ML models, with an AUROC of 0.800 and F1 measure of 0.441. RF and XGB algorithms showed AUROC values similar to GUSS (0.794 and 0.791, respectively). The modified Rankin scale, days to initial VFSS, and facial asymmetry were the top three important predictors of ML performance.

**Conclusion:** The proposed ML prediction models are valid and applicable for screening aspiration in patients with acute stroke. The RLR showed the best performance among the models, suggesting that it could alternate existing screening tools.
On-demand oral presentation

0-50 Effects of the ultrasound and sonic toothbrushes on oral hygiene and dysphagia in convalescent post-stroke patients: A randomized controlled study

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Background: In stroke, patients have both sensory and motor deficits. Oral care is often overlooked during stroke rehabilitation. Physical weakness, lack of coordination and the cognitive problems that can accompany a stroke may prevent a person from maintaining good oral hygiene on their own.

Objectives: To investigate the effects of the ultrasound and sonic toothbrushes in patients after stroke.

Design: Randomized, controlled study.

Setting: Four convalescent rehabilitation hospitals.

Interventions: Post-stroke patients were randomly allocated to control or experimental group. The experimental group used with the ultrasound and sonic toothbrushes, and the control group used toothbrushes with power off (without ultrasound and sonic wave). Oral care was performed three minutes per session, twice a day, seven times per week, for twelve weeks.

Main Outcome Measures: Simplified Oral Hygiene Index (S-OHI), Plaque Index (PlI), Gingival Index (GI), Saxon test (saliva secretion), Functional Oral Intake Scale (FOIS) and questionnaire were recorded before, and 12 weeks after each intervention.

Results: Forty subjects were enrolled in this study. At baseline, oral hygiene status in post-stroke patients was poor. And also, the amount of saliva was small, dysphagia was remarkable. In both groups, all outcome measures were improved after the intervention. However, there were significant differences between the experimental and control group for S-OHI, PlI, GI, Saxon test, FOIS and patient satisfaction, 12 weeks after the intervention.

Conclusion: These findings demonstrate that the use of ultrasound and sonic toothbrushes effectively decreased the poor oral hygiene, and increased saliva secretion. Professional prophylaxis was required to improve gingival status. Oral care with ultrasound and sonic toothbrushes, is superior to conventional treatment alone for post-stroke patients.
On-demand oral presentation

**0-51 Gender differences in mortality and functional outcomes after the first-ever stroke: a multicenter prospective cohort study**

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This study aimed to determine whether there are gender differences in mortality and functional outcomes up to the five years after first-ever stroke. This is an interim analysis of the Korean Stroke Cohort for Functioning and Rehabilitation (KOSCO), a prospective multicenter cohort study. Multifaceted functional assessments were performed repeatedly from 7 days to 60 months after stroke onset using the Fugl–Meyer Assessment (FMA), the Functional Ambulation Classification (FAC), the American Speech–Language–Hearing Association’s National Outcomes Measurement System (ASHA-NOMS), the Short Korean version of the Frenchay Aphasia Screening Test (Short K-FAST), the Korean Mini-mental Status Examination (K-MMSE), and the Korean-Modified Barthel Index (K-MBI). Gender-related differences in mortality and long-term functional recovery were analyzed using Cox regression models, analysis of covariance, and generalized estimating equations (GEEs). Of 10,636 first-ever stroke patients (n=4,595 or 43.2% female) admitted to nine representative hospitals in Korea, 7,858 patients (3,315 or 42.2% female) who gave informed consent were included in this analysis. There was significant gender difference in mortality rate only in ischemic stroke (IS) patients after correction for possible covariates. Among them, 4,443 patients (1,794 or 40.4% female) completed functional assessments until 60 months. After adjustments, female IS patients showed lower FAC, K-MMSE, short K-FAST, and K-MBI scores. The GEE analysis indicated significantly poorer recovery of the K-MBI scores in females. In contrast, females had significantly higher FMA scores and lower swallowing functions than males after hemorrhagic stroke (HS). Results of this study showed gender differences in some functional domains and recovery pattern in IS and HS patients and suggested the need of gender-specific long-term management strategies to reduce the disability burden of such patients.

**Funding**

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On-demand oral presentation

0-52 Effects of neuromuscular electrical stimulation for treatment of dysphagia in acute stroke patients: A Randomized Controlled Trial

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The purpose of this study was to compare the effects of a novel neuromuscular electrical stimulation (NMES) to the effects of conventional treatment in patients with dysphagia after stroke. Patients with acute stroke were randomly allocated to an NMES, or a control group. Participants received either 20 sessions of NMES at the motor point of the target muscles, or conventional treatment in each group for 4 weeks. The NMES group received NMES intervention followed by conventional treatment, including thermal-tactile stimulation with intensive repetition of a dry-swallow task. The control group received conventional treatment without NMES. NMES at a fixed pulse duration of 50 μs and a frequency of 50 Hz was delivered over the skin areas above the motor point of the target muscles, i.e., the bilateral geniohyoid, mylohyoid/anterior belly of the digastric, and thyrohyoid muscles, using a high-voltage pulsed-current device. The two groups received 40-min treatments once a day, 5 days per week, for 4 weeks. Outcome, assessed before and 4 weeks after treatment, was evaluated with regard to the videofluoroscopic dysphagia scale (VDS), the anterior and superior displacement of the hyoid bone and larynx, and the functional oral intake scale. Thirty-six participants were enrolled (18 and 18 respectively in the NMES, and control groups) and all participants completed the trials. Both groups exhibited improvement, but the NMES group exhibited more significant improvement in the displacement of the hyoid bone and larynx, VDS-total score, and VDS-pharyngeal score than the control group did. The results suggest that NMES combined with conventional treatment is superior to conventional treatment alone in patients with dysphagia following treatment for brain injury. Further investigations are necessary to examine the effects of NMES in patients with more varied types of diseases.
On-demand oral presentation

**O-53  Antithrombotic therapy and recurrent stroke before PFO closure**

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**Background**
The transcatheter closure of a patent foramen ovale (PFO) reduces the risk of recurrent stroke, particularly PFO-associated with cryptogenic stroke (PFO-CS). In general, antiplatelet therapy started prior to PFO closure for CS patients without venous thromboembolism (VTE). Our aim was to clarify the association between antithrombotic therapy and recurrent stroke.

**Method**
We retrospectively enrolled stroke patients who underwent PFO-closure, and collected data of antithrombotic therapy (antiplatelet, AP group/ anticoagulant, AC group) and recurrent stroke. Our first-line antithrombotic therapy is antiplatelet agent for PFO-CS patients without VTE. A high-risk PFO was defined as 1) large right-to-left shunt, and/or 2) atrial septal aneurysm and/or hypermobile interatrial septum.

**Results**
A total of 17 patients were enrolled (median 60 years old; male, 65%; >60 years old, 65%; RoPE score>6, 41%). Sixteen patients (94%) had a high-risk PFO, and the interval between index stroke and PFO closure was 153 days (median). Of the 7 patients in AP group, 3 patients (43%) had recurrent stroke before PFO-closure. Of 11 patients in AC group, no one had recurrent stroke before PFO-closure. The reasons for anticoagulants were VTE (n=7) and physicians’ selection that anticoagulant is preferable despite no VTE (n=4). After PFO-closure, no one developed recurrent stroke.

**Conclusion**
Approximately 40% of patients had recurrent stroke before PFO-closure in AP group. We might need to reconsider antithrombotic agents before PFO-closure even without overt VTE.
On-demand oral presentation

**0-54 A case of cardioembolic stroke with calcified amorphous tumor (CAT)**

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CAT is a non-neoplastic tumor of the heart with amorphous fibrous material, which may cause cerebral infarction. Here, we report a case of a 69-year-old right-handed man. His chief complaint was difficulty in speaking. One day, at 0:00 PM he suddenly noticed difficulty in speaking and visited a local doctor. Cerebral infarction was suspected, and he was referred to our hospital at 5:00 PM. Neurological examination revealed only motor aphasia with NIHSS 1. Brain MRI showed acute cerebral infarction in the left frontal lobe and subacute cerebral infarction in the right frontal lobe. MRA showed interruption at left M2. Aphasia was so mild that endovascular treatment was not given. After admission, transthoracic echocardiography showed calcification of the mitral valve. Transesophageal echocardiography, CT, and cardiac MRI revealed CAT with a maximum diameter of 2 cm attached to the posterior leaflet of the mitral valve. No other sources of embolism were found throughout the body. Tumor resection with mitral valve replacement was performed by the cardiovascular surgery team. The contents overflowed from the tumor when the tumor was resected. Inflammatory cell infiltration and calcification were found in the tumor wall by the pathology. Until today, 18 cases of CAT induced cerebral infarction have been reported, mostly from Japan. More CAT cases may be overlooked. Antithrombotic treatment may not prevent recurrence of cerebral infarction, therefore aggressive surgical treatment is required in most cases.
Background: The impact of pre-admission treatment on prognosis after stroke is challengeable. This study aimed to investigated whether pre-admission use of anti-platelets agents was associated with mortality in patients with cerebral infarction.

Methods: We used hospital-based registry to identify all patients with first-time stroke, who admitted to a tertiary hospital located in metropolitan area of South Korea, and subsequent mortality in patients treated with anti-platelets therapy during 2017-2020. We examined 90-day mortality for current anti-platelets therapy and non-users. We used Cox regression to control for potentially confounding factors.

Results: Among anti-platelets therapy, 90-day stroke mortality was 0.908 (95% confidence interval (CI) 0.845-1.278) for all single anti-platelets therapy and 2.013 (95%CI 0.842-4.814) for any oral anti-coagulations. In contrast, any dual anti-platelet therapy was associated with 90-day mortality (2.181, 95%CI 1.337-3.558).

Conclusions: Among patients with first-time stroke, pre-admission dual anti-platelets therapy was associated with increased 90-day mortality. Further prospective studies of these medications on ischemic stroke and early prognosis are needed.
On-demand oral presentation

O-56  Prestroke antiplatelet therapy and initial stroke recurrence

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**Background:** The effect of pre-stroke use of antiplatelets on initial stroke recurrence is uncertain. Therefore, this study investigated whether pre-admission use of anti-platelet agents was associated with initial stroke recurrence in patients with cerebral infarction.

**Methods:** Between March 2017 and December 2020, patients admitted to a tertiary hospital located in metropolitan area of South Korea, due to ischemic stroke were included. A total of 1,877 patients (60.9% men, mean age 65.42±13.64 years) who had undergone brain MRI were selected with demographic, clinical, and laboratory data, including pre-stroke medications and clinical course. We examined 90-day stroke recurrence for current anti-platelets therapy and non-users. We used Cox regression to control for potentially confounding factors.

**Results:** Among anti-platelets therapy, 90-day stroke recurrence was 1.137 (95% confidence interval (CI) 0.591-2.185) for all single anti-platelets therapy, 0.800 (95%CI 0.281-2.279) for any dual anti-platelets therapy, and 1.047 (95%CI 0.107-10.263) for anti-coagulations.

**Conclusions:** Among patients with first-time stroke, prestroke anti-platelets therapy and anti-coagulations was not associated with increased initial stroke recurrence.
Background: Hypertriglyceridemia can promote atherosclerotic pathology, but its role in stroke has not been well defined. We aimed to assess the contribution of hypertriglyceridemia to residual vascular risk in patients with stroke or transient ischemic attack (TIA).

Methods: The Tokyo Women’s Medical University Stroke Registry is an ongoing prospective, observational registry, in which 870 patients with acute ischemic stroke or TIA within 1 week of onset were consecutively enrolled and followed up for 1 year. Hypertriglyceridemia was defined as serum triglycerides levels of ≥150 mg/dL under fasting conditions. Significant stenosis of the cervicocephalic arteries was defined as having ≥50% stenosis or occlusion. The primary outcome was major adverse cardiovascular events (MACE), including nonfatal stroke, nonfatal acute coronary syndrome, and vascular death.

Results: Of 870 patients (mean age, 70.1 years; male, 60.9%), 217 (24.9%) had hypertriglyceridemia. High triglycerides levels were significantly associated with an increased prevalence of intracranial artery stenosis, particularly in the anterior circulation, rather than extracranial artery stenosis. Patients with hypertriglyceridemia had a greater risk of MACE than those without (annual rate, 20.9% vs. 9.7%; \( P < 0.001 \)), even after adjustment for potential confounders, including baseline low-density lipoprotein cholesterol and statin use (adjusted hazard ratio, 2.46; 95% confidence interval, 1.62-3.74). The higher risk of MACE in hypertriglyceridemia versus non-hypertriglyceridemia patients was observed among patients with stroke of atherothrombotic origin (n=174; annual rate, 35.1% vs. 14.2%; \( P = 0.001 \)), those with significant intracranial artery stenosis (n=247; annual rate, 29.9% vs. 14.7%; \( P = 0.006 \)), and those with significant extracranial carotid artery stenosis (n=123; annual rate, 23.0% vs. 9.4%; \( P = 0.042 \)). In contrast, hypertriglyceridemia was not predictive of recurrent vascular events in patients with cardioembolic stroke (n=221; annual rate, 19.1% vs. 10.5%; \( P = 0.18 \)).

Conclusions: Hypertriglyceridemia is an important modifiable risk factor that drives residual vascular risk in patients with stroke of atherothrombotic origin, even while on statin therapy.
On-demand oral presentation

0-58 Arachidonic acid level is related to motor recovery in intracerebral hemorrhage with severe motor paralysis

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Background and Purpose: Factors associated with recovery of severe motor paralysis in patients with intracerebral hemorrhage (ICH) remains unclear. Some polyunsaturated fatty acids (PUFAs) are said to be related with the prognosis of ICH. We aimed to determine the association between serum PUFAs level and motor recovery in ICH with severe motor paralysis.

Methods: Consecutive ICH patients admitted to our hospital between October 2012 and December 2021 were screened. Inclusion criteria were: 1) patients with an average of upper and lower extremity National Institutes of Health Stroke Scale (NIHSS) sub-score 3-4 on admission; 2) able to evaluate NIHSS score on day 7 of hospitalization; and 3) able to measure PUFAs within 7 days from the admission. We defined a recovery of severe motor paralysis as an average of upper and lower extremity NIHSS sub-score 0-2 on day 7 from the admission. We evaluated whether PUFAs level could be associated with a recovery of severe motor paralysis.

Results: We screened 377 consecutive ICH patients, including 121 patients (75 (62%) male, median age 64 years). A recovery of severe motor paralysis was seen in 39 patients (32%). In multivariable logistic regression analysis, and higher arachidonic acid (AA) level was independently associated with a recovery of severe motor paralysis (odds ratio (OR) 2.284, 95% confidence interval (CI) 1.016-5.131, \( p = 0.046 \), Figure). Further, in multivariable logistic regression analysis using AA tertile with and without a recovery of severe motor paralysis, a linear trend was observed between the tertile of AA and a recovery of severe motor paralysis in reference to AA Tertile 1 (AA Tertile 2: OR 1.402, 95% CI 0.426-4.614, \( p = 0.578 \), and AA Tertile 3: OR 3.226, 95% CI 1.043-9.973, \( p = 0.042 \)).

Conclusions: Higher AA level is associated with a recovery of severe motor paralysis in patients with intracerebral hemorrhage.
On-demand oral presentation

O-59  Serum mucin levels are related with large thrombus formation as well as hypercoagulability in the cancer-associated stroke

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Background: Although direct factor Xa inhibitors (DXaI) have been demonstrated to be effective in prevention of venous thromboembolism (VTE), its effectiveness in arterial thromboembolism including cancer-associated stroke (CAS) still remains unclear. Because non-bacterial thromboendocarditis is often related with adenocarcinoma, we thought to elucidate roles of mucin molecules in thrombogenesis.

Subjects and methods: We enrolled 56 sequential patients with CAS (age 76.5±10.4 years, 25 males and 31 females) retrospectively. Fifty two out of 61 cancers (92.9%) were adenocarcinomas. We tried to determine correlation between serum mucin levels and coagulation markers and compared these markers in large-sized territorial stroke (n=10) with those in small scattered infarctions (n=24) in brain MRI. Furthermore, we examined incidence of stroke recurrence in patients treated with unfractionated heparin (UFH, i.v. or s.c., n=13) or in those under DXaI treatment (n=13).

Result: 1) There was a significant correlation between D-dimer and CA19-9 (Pearson’s coefficient: 0.40649) or CA125 (0.5017). 2) Serum CA125 levels in patients with large infarcts (702.0±1433.4 ug/mL) were increased compared with those with small infarcts (395.2±762.5 ug/mL), while D-dimer in the large infarct group (28.9±17.6 ug/mL) were comparable with those in the small infarct group (22.9±22.3 ug/mL). 3) No recurrent stroke was detected in the UFH group, while 2 patients in the DXaI group were suffered from recurrence. Two patients in each group terminated their anticoagulants for hemorrhagic events, and 2 in the UFH group were complicated with heparin-induced thrombocytopenia.

Discussion: Serum mucin levels were correlated with hypercoagulability as well as large thrombus formation. These data suggested that the circulating mucin may be involved in thrombogenesis not only by activating prothrombin directly, but also by facilitating selectin-mediated interactions among platelets, monocytes, and endothelial cells (Varki A, 2007). Because the latter mechanism is inhibited only by heparin, it might be more promising for prevention of CAS recurrence.
Radiotherapy for brain tumors is an established treatment, but it carries the risk of serious complications. We herein report two cases of progressive intracranial carotid artery stenosis after radiation therapy for brain tumors, which are successfully treated by extracranial-intracranial (EC-IC) bypass.

Case 1: A child with Down's syndrome presented with right hemiplegia. Stereotactic biopsy revealed a mixed germ cell tumor in left basal ganglia. He underwent whole brain and local irradiation. Five years later, MRA showed rapidly progressing stenosis of the intracranial left internal carotid artery (ICA). Although asymptomatic, IMP-SPECT showed extensive cerebrovascular reserve impairment in the left cerebral hemisphere, so left combined EC-IC bypass surgery was performed to avoid future stroke. Case 2: A male in his 40s was diagnosed with atypical meningioma in third ventricle. He underwent local irradiation of the residual tumor. Four years later, he presented disorientation and poor vitality; MRA showed stenosis of the terminal portion of the left ICA and IMP-SPECT showed extensive hypoperfusion of the left cerebral hemisphere. He underwent left ECA-RA-M2 bypass, which resulted in symptomatic improvement.

Radiation-induced intracranial ICA stenosis can occur in patients with brain tumor treated with radiation therapy. Although radiation-induced intracranial ICA stenosis is relatively uncommon, it is progressive and may cause cerebral infarction. Regular evaluation of intracranial artery following radiation therapy is necessary and early surgical intervention using EC-IC bypass might be useful.
On-demand oral presentation

0-61 Symptomatic steno-occlusion and recurrence in acute ischemic stroke patients with atrial fibrillation

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Background and Aims: Symptomatic cerebral arterial steno-occlusion (SYSO) has a clinical impact on the outcome of acute ischemic stroke (AIS). SYSO is prevalent in patients with AIS and atrial fibrillation (AF) as well. This study investigated the association between SYSO and recurrence in AIS patients with AF.

Methods: This study was a case-cohort study from a prospective cohort of 2,287 AIS patients with AF from 14 stroke centers in the South Korea. Amongst the participants of the cohort, we identified 95 patients with recurrent ischemic stroke during the follow-up and selected randomly sampled 114 patients (5%) as a subcohort for comparison. We define symptomatic steno-occlusion as more than 50% stenosis or occlusion of cerebral arteries proximal to single-territorial infarction area. Symptomatic and all cerebral arterial steno-occlusion were evaluated with MR or CT angiography. Weighted Cox proportional hazard model was analyzed to evaluate the association between steno-occlusion and recurrence with adjusting vascular risk factors and discharge anticoagulant use.

Results: The case group had more SYSO (29% vs. 19%, p=0.008) and any steno-occlusion (82% vs. 62%, p=0.004) compared to the control group. In multivariable analysis, SYSO increased the risk of recurrence (Adjusted hazard ratio 3.37, [95% confidential interval 1.47-7.76],p=0.004) and any steno-occlusion also elevated the risk (3.06, [1.52-6.16], p=0.002). Irrelevant cerebral arterial stenosis also increased the risk of recurrence (2.88, [1.37-6.09], p=0.006).

Conclusions: Our findings suggest that any steno-occlusion, especially SYSO increased the recurrence risk in AIS patients with AF by more than 3 times, and should be considered in the prediction of recurrence risk in AIS patients with AF.

Acknowledgement: We would like to show our gratitude to institutions provide us the opportunity to analyze EAST-AF-Part II and CRCS-K database for this study.
On-demand oral presentation

**O-62 Comparisons of HATCH, HAVOC and CHA2DS2-VASc scores for all-cause mortality prediction in atrial fibrillation: a real-world evidence study**

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**Objective:** This study focused on the predictive ability of the 3 scores for all-cause mortality in 6444 patients with atrial fibrillation (AF).

**Methods:** To assess the predictive accuracy of risk of death modelled by HATCH, HAVOC and CHA2DS2-VASc scores, the area under the curve of receiver operating characteristics (AUROC) was applied.

**Results:** Over follow-up time, the cumulative incidence of death was clearly associated with the three scores (log-rank test, p<0.001). The AUROC for the HATCH (0.6618) was significantly higher than HAVOC Score (0.5733) and CHA2DS2-VASc Score (0.6423).

**Conclusions:** HATCH score has better ability in predicting mortality in comparison to other two scores in patients with AF.
On-demand oral presentation

0-63  Baseline platelet count may predict short-term functional outcome of cerebral infarction

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Background and aims: Platelets not only play an important role in the coagulation system, but they have also been implicated in the mortality after myocardial infarction. In the present study, we investigated whether platelet count is associated with differences in the short-term prognosis at the time of hospital discharge and early neurological deterioration in ischemic stroke.

Methods: Patients with ischemic stroke were enrolled from among 661 cerebrovascular disease patients admitted between January 2018 and December 2020. Patients who received hyperacute treatment, had a pre-onset modified Rankin scale (mRS) ≥3, transient ischemic attack, or active malignant disease were excluded. The platelet count was divided into quartiles (Q1-4) according to the number of patients, and the relationship between platelet count and prognosis was assessed using multivariate analysis.

Results: In total, 385 patients were included in the study. Regarding the functional outcome by platelet count, there was a significant increase in mRS≥3 at discharge in the Q1 (range; 19-173 x 109/L) and Q4 (range; 243-1327 x 109/L) groups compared with the Q3 (range; 205-242 x 109/L) group even after adjusting for background, vascular risk factors, and pre-medications. Furthermore, the frequency of neurological deterioration (NIHSS ≥ 4) within 1 week was significantly lower in the Q3 group than in the Q1 and Q4 groups even after adjustment (p<0.05).

Conclusion: Platelets release trophic factors, which are useful in platelet-rich plasma treatment. This study may help clarify the pathogenesis of cerebral infarction to improve the prognosis.
On-demand oral presentation

**O-64 Differences in recurrence rates of cardioembolic stroke according to the type of statin used in patients with stroke caused by atrial fibrillation**

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**Background**

Many studies suggest regarding pleiotrophic effect of statin in the prevention and treatment of AF. However, there is no clinical studies comparing effect between types of statins. This study investigated the association of types of statins with preventive effect on AF induced cardioembolic stroke.

**Methods**

Consecutive patients with acute cerebral artery infarction due to atrial fibrillation from January 2017 to May 2019 were encountered in a single stroke center. Three groups were retrospectively revised for 2 years based on medical records (Group 1- NOAC only, Group 2- NOAC plus statin, Group 3- NOAC plus statin and ezetimibe). Two study object were observed. First, stroke recurrence among three groups in follow up period were compared. Second, stroke recurrence between two statin group (atorvastatin or rosuvastain) with or without ezetimibe were evaluated. Kaplan-Meier curve analysis and log rank test were used to compare incidence among three groups and T-test were used to compare incidence between atorvastatin and rosuvastain groups.

**Result**

A total of 73 patients were classified into three groups (24, 27 and 22 in group 1, 2, 3 respectively). Patient characteristics were not different among three groups. After 2 years of follow up period, 11 (45.8 %), 8 (29.6 %) and 7 (31.8 %) recurred stroke from atrial fibrillation in group 1, 2, and 3 respectively (p<0.05) (figure 1). There was no Inter-group difference between group 2 and 3. Instead, stroke recurrence between atorvastatin and rosuvastain group showed statistically significant difference (atorvastatin (24%) 6 out of 25 vs. rosuvastain (41.7%) 10 out of 24) (p<0.05).

**Conclusion**

Atorvastain showed more preventive effect on ischemic stroke recurrence from atrial fibrillation than rosuvastain, which implies statin type could give affect on atrial fibrillation related stroke. Further studies with large number and randomized prospective study are needed.
The ED coil-10 is an extremely soft coil with an for embolization of the ED soft coil has been improved as “i-ED coil”. I-ED soft coils are soft and suitable for finishing with less kickback. The i-ED 14 Infini coil is a 0.014-inch, less shaped memory coil, and is suitable for stent-assisted embolization of cerebral aneurysms. We report on their utility.

The i-ED coils were used in 46 patients; ruptured, 8) between January 2020 and December 2020 in our hospital.

The i-ED soft coils were mainly used as the finishing coil, and the i-ED 14 Infini coils were used.

The i-ED soft coils are extremely soft and suitable for the finishing stage of embolization. The i-ED 14 Infini coil seeks the open space in the aneurysms regardless of the size and shape of the coils (30cm and 50 cm) regardless of the secondary coil diameter can be selected.
On-demand oral presentation

0-66 Adenomyosis: an emerging risk factor for embolic stroke of undetermined source in middle-aged women

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Background: Adenomyosis is a benign condition of the uterus. We previously reported 4 cases of cerebral infarction associated with adenomyosis in 2012. Since then, similar cases in Asia have been reported. The clinical features and potential mechanisms of cerebral infarction were examined in patients with adenomyosis.

Methods: PubMed was searched for all case reports of cerebral infarction associated with adenomyosis in English until December 2021 using the keywords ‘adenomyosis’ and ‘cerebral infarction’.

Results: Patients with cerebral infarction associated with adenomyosis have been reported from Japan, South Korea, and China, with a total of 18 cases including ours. The mean age at onset of cerebral infarction was 45.9 (range: 34-59) years. Cerebral infarction developed during menstruation in 64.7% of patients. Serum CA125 levels (median 735.7 U/mL, range 42.6-3536 U/mL) were increased in all patients, and plasma D-dimer levels (median 4.0 μg/mL, range 0.57-79.3 μg/mL) were increased in all patients except one. Cerebral infarction was observed in multiple vascular territories in 67% of patients, 39% had systemic thromboembolism, and 22% had nonbacterial thrombotic endocarditis. All 4 patients treated with GnRH agonists for adenomyosis showed recurrence of cerebral infarction after discontinuation of GnRH agonist treatment with increased CA125 and D-dimer levels. In patients who underwent hysterectomy, CA125 and D-dimer levels decreased or normalized, and no recurrence of cerebral infarction was observed. Embolic stroke in adenomyosis might be caused by the following mechanisms: 1) P- and L-selectin activation with mucins (CA125); 2) increased tissue factor expression in adenomyosis lesions; 3) nonbacterial thrombotic endocarditis; 4) menstruation-related coagulopathy; or 5) severe iron deficiency anemia.

Conclusion: Accumulating evidence suggests that adenomyosis is one of the causes of embolic stroke of undetermined source in middle-aged women, particularly in those with highly elevated CA125 levels.

Possible underlying mechanisms of embolic stroke of undetermined source with adenomyosis in middle-aged women

- P- and L-selectin activation with mucins (CA125)
- Increased tissue factor expression in adenomyosis lesions
- Nonbacterial thrombotic endocarditis
- Menstruation-related coagulopathy
- Severe iron deficiency anemia.
On-demand oral presentation

**0-67 Temporal muscle thickness predicts severe prolonged post stroke dysphagia in acute ischemic stroke**

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**Background**
Post stroke dysphagia (PSD) is a common complication after stroke. Temporal muscle thickness (TMT) was affected by nutrition state and associated with prolonged PSD in ischemic stroke patients. However, there was no optimal cutoff value of TMT for predicting prolonged PSD and the association of TMT with other confounding factors for PSD have not been verified.

**Methods**
We conducted retrospective analysis of ischemic stroke patients in our institute from January 2019 to December 2019. TMT was obtained from source image of time-of-flight magnetic resonance angiography (TOF-MRA) after admission. Swallowing state was assessed at discharge using food oral intake scale (FOIS). FOIS level 1-3 was defined as severe PSD. As for nutrition state, geriatric nutritional risk index (GNRI) was also calculated. The association between TMT and severe PSD state was assessed.

**Results**
Of 251 patients (median age, 74 years; male, 57%, median TMT 6.89mm), severe PSD was detected in 33 patients. Patients with severe dysphagia showed older age, higher pre-mRS score, lower GNRI, and higher NIHSS score. TMT was also thinner in severe PSD. Area under the curve (AUC) of TMT for severe PSD was 0.69 (95% CI 0.58-0.81) with cutoff value of 6.2mm. On the logistic regression analysis, TMT under cutoff value showed significantly associated with severe PSD (TMT<6.2mm, adjusted OR 2.92, 95%CI 1.02–8.36).

**Conclusions**
In ischemic stroke patients, TMT under 6.2mm was independently associated with severe PSD, suggesting TMT measurement at admission could stratify the patients with the risk of prolonged PSD.
On-demand oral presentation

0-68 Potential application of regenerative associated cells including endothelial progenitor cells for the treatment of acute cerebral infarction

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Purpose: Recently, we have developed quality and quantity-controlled (QQ) culture systems to obtain mononuclear cells enriched in endothelial progenitor cells (EPCs) with well-defined angiogenic and anti-inflammatory phenotypes. These cultured cells are called regenerative associated cells (RACs). Using the RACs, we evaluated the condition of RACs in the patients with acute cerebral infarction (ACI) by onset time.

Subjects and Methods: Peripheral blood samples were collected from 39 patients with ACI admitted to our hospital within 24 hours, 24-48 hours, 48-72 hours, and approximately 10 days after the onset of stroke. We measured CD206, CD34, and CD133 in QQ cultured cells of patients with ACI. CD206 was used as a marker for M2 macrophages. EPCs are abundant in the group of cells in which both CD34 and CD133 are positive. As for these cultured cells, cytokine assay (IL-10 and TNF-α) were also performed. 25 age-matched non-stroke volunteers performed the same analysis as a control.

Results: The percentages of both positive cells of CD34 and CD133 before QQ cultures were higher in ACI group (48-72h) than in control group, while there were no significant differences between both groups after QQ cultures. The percentage of CD206 positive cells before QQ cultures significantly increased in the ACI group, especially in the 0-24h and 24-48h groups after QQ cultures. The Ratio of IL-10 to TNFα level were higher in the ACI group (24-48h, 48-72h) before QQ cultures, and it was even higher after QQ cultures.

Conclusion: In the patients with ACI, the number of CD34 and CD133 positive cells increased from 48 to 72 hours after stroke onset, and the ratio of IL-10 to TNFα level increased from 24 to 72 hours after stroke onset. These findings suggest that RACs in the patients with ACI might have high potential ability of vascular regeneration.
On-demand oral presentation

**0-69  Upbeat nystagmus and central positional nystagmus associated with thalamic infarction**

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**Background:** Spontaneous upbeat nystagmus, apogeotropic horizontal nystagmus on supine roll test, and positional downbeat nystagmus are considered red flags for central vertigo. We report a patient with spontaneous upbeat nystagmus followed by positional nystagmus occurring in more than one plane associated with thalamic infarction.

**Case report:** A 61-year-old man noted acute onset of vertigo and nausea on awakening. He did not notice associated hearing loss or tinnitus. He presented to the emergency department 4 hours after the onset. On examination, the patient was alert. He could not stand because of truncal ataxia, but there was no limb dysmetria. Eye movements were normal. Upbeat nystagmus was present with the eyes in central position. Horizontal gaze-evoked nystagmus was also present. Diffusion-weighted magnetic resonance imaging (MRI) revealed left thalamic infarction. Video-oculography performed one day later showed a spontaneous left-beating nystagmus with eyes open in darkness. Supine roll test to either side showed apogeotropic nystagmus but resulted in vertigo in the right ear dependent position only. Bilateral Dix-Hallpike maneuvers resulted in positional downbeat nystagmus without vertigo. A reversion of the nystagmus direction to upbeat with vertigo was observed when he sat up from the supine position. A left canal paresis of 73% was found. Cervical vestibular evoked myogenic potentials were absent from the left ear. Video head impulse tests performed 4 days after admission were normal. The vertigo gradually improved over the subsequent week.

**Conclusion:** Upbeat nystagmus has been reported with midbrain and thalamic abnormalities. Although midbrain infarction was not present on MRI, the function of midbrain might have been compromised by the thalamic infarction. In addition, the thalamic infarct may cause central positional nystagmus occurring in more than one plane.
Objective: The aim of this study was to investigate the association between ischemic or hemorrhagic events and oral antithrombotic treatments in patients with non-valvar atrial fibrillation (NVAF) who underwent carotid artery stenting (CAS).

Methods: We retrospectively enrolled NVAF patients who underwent CAS from April 2005 to August 2021 at 12 stroke centers in Japan. The association between the oral antiplatelets (APT) or anticoagulants (AC) and the frequency of ischemic stroke, major bleeding, cardiovascular death, and in-stent restenosis at 6 months and 1 year after the procedure were investigated.

Results: We enrolled 138 patients in this study. The content of oral antithrombotic treatment 6 months after CAS were as follows: AC+dual APT (DAPT) was 47%, AC+single APT (SAPT) 39% on, AC only 7%, APT only 6%, and AC+triple APT (TAPT) 1%. Up to 1 year after CAS, AC+SAPT was 62%, AC only 20%, AC+DAPT 12%, and APT only 5%. During the follow up period, 13 of ischemic strokes, 14 of major bleedings, 7 of cardiovascular deaths, and 18 in-stent restenosis occurred. In multivariable regression analysis, patients with AC+DAPT had the lowest frequency of major bleedings (odds ratio (OR) 0.06 p<0.01), cardiovascular death (OR 0.07 p=0.04), and composite events (OR 0.13, p=0.02) compared to AC alone at 6 months after CAS. At 1 year after CAS, patients on AC+SAPT had the lowest frequency of major bleeding (OR 0.11 p=0.02) and composite events (OR 0.26 p=0.02).

Conclusion: In patients with NVAF who underwent CAS, patients with AC+DAPT had the lowest frequency of major bleeding, cardiovascular death, and all composite events at 6 months after CAS and patients with AC+SAPT had the lowest frequency of major bleeding and all composite events at 1 year after CAS.
Background and Purpose: The outbreak of the novel coronavirus disease (COVID-19) significantly impacted stroke care, which requires a rapid response. In our hospital, three neurologists are available to treat emergency patients with suspected stroke in the hyperacute phase, and a stroke code of MRI-first is in place. The "COVID-19 stroke code", a newly designed stroke code at our hospital, is used for patients who are suspected of having complications of COVID-19 infection and it is performed by CT-first. Stroke mimics (SM) are always present in a certain number of patients, making acute stroke treatment more complicated. Here, we describe the clinical characteristics of patients with SM among those who underwent stroke code at our hospital.

Methods: The period from April 2018 to April 2019 was defined as pre-COVID-19 pandemic, and that from October 2020 to April 2021 as COVID-19 pandemic period. Among the emergency transport cases with stroke code activated, the SM cases were selected, and their clinical characteristics, door to image time (DTI), and other characteristics were evaluated retrospectively.

Results: Of the 425 cases, 66/192 and 57/233 were SM cases before and during the COVID-19 pandemic, respectively, showing that it was significantly fewer during the pandemic period than pre-COVID-19 pandemic, (24.5% vs. 34%, \(p<0.05\)). "COVID-19 stroke code" was performed in 54/233 (23%) cases, of which 15 were SM cases. DTI in SM cases with "COVID-19 stroke code" was not significantly different from pre-COVID-19 pandemic [median (IQR) 17 (11.5–19) min vs. 19 (14.25-25) min, \(p>0.05\)].

Conclusion: The number of SM cases during the COVID-19 pandemic was few, and although "COVID-19 stroke code" was performed as CT-first, no difference in time compared with that of the normal stroke code, which was MRI-first, was noted.
On-demand oral presentation

0-72  A case of septic cavernous sinus thrombosis complicated with tuberculosis and acute ischemic stroke

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1. Introduction
Septic cavernous sinus thrombosis (SCST) is an uncommon condition and the mortality rate is known to be high. We report a very rare case of SCST complicated with tuberculosis and acute cerebral infarction.

2. Case
A 66-year-old male patient visited the emergency room with symptoms of left ptosis. On neurologic examination, paralysis of the extraocular muscle in the left eye was observed. In laboratory tests, C-reactive protein was elevated to 17 mg/dL and chest CT showed peribronchial nodules and consolidation in the left upper lobe. On MRI, a gadolinium contrast filling defect was observed in the left cavernous sinus, suggesting thrombosis. Acute infarctions of embolic pattern were observed in the left hemisphere with severe stenosis in left proximal ICA. Also, sphenoidal sinusitis was observed. One day later, the patient became drowsy and right hemiplegia developed. Follow-up MRI showed newly developed left T-ICA severe stenosis and exacerbation of cerebral infarct lesions. Emergency intervention was attempted and left carotid stent insertion and intracranial stent insertion were performed. However, the patient's symptoms did not improve, and M.tuberculosis PCR was confirmed in the sputum. Standard anti-TB drugs were started, and evaluation of the causative microbiology of sphenoidal sinusitis was considered, but biopsy could not be performed because antiplatelet and anticoagulant agents were simultaneously administrated. Respiratory hold occurred on the 9th day of admission, but the caregiver did not want further treatment, and the patient died.

3. Discussion
It is known that SCST is mainly caused by the spread of infections originating in the face and paranasal sinuses, but reports of tuberculous SCST are very rare. In the case of the patient, sputum PCR confirmed M.tuberculosis, but it was not possible to prove whether M.tuberculosis caused SCST.
A 65-year-old male was admitted to the stroke-ward following dysarthria, right-side motor weakness and sensory loss. Three months ago, the patient had been hospitalized because of acute cerebral infarction in multiple territory and diagnosed that he also had a LEMS.

Past medical history included hypertension, dementia (MMSE 18), Dyslipidemia. On neurological examination, apart from the pre-existing mild left-sided lower extremity weakness (MRC Gr4), he was also newly exhibited left-sided motor weakness (upper Gr3, lower Gr3), partial sensory loss at the left-side and central type of facial palsy on the left face. General examination showed skin lesion which looked like livedo reticularis involving both lower legs.

The patient had taken clopidogrel well; platelet function EPI 241 and ADP 133. Cerebral MRI showed diffusion restrictive lesion in left internal capsule posterior limb and right inferior frontal lobe. Follow-up cerebral angiography confirmed mild stenosis of left carotid bulb, VA, proximal MCA and right distal ACA.

Cardiac ultrasonography showed normal cardiac function. 24hr Holter-monitoring revealed basically normal sinus rhythm with few premature atrial contractions.

Laboratory research for tumor marker revealed all negative furthermore chest, abdomen and pelvis CT did not show any findings suggestive of cancer. There were high level of rheumatoid factor(>650IU/ml) and antiphospholipid immunoglobulin G(25.1 GPL/ml) in serum. The skin biopsy obtained from the right leg confirmed melanin incontinence throughout the dermis and minimal superficial perivascular lymphocytic infiltrate.

We considered the possibility of SS and changed the medication for prevention of recurrent stroke to warfarin.

This case is about an old male who had a possibility of Sneddon syndrome accompanied by LEMS. We recommend that if a patient has skin lesion that is a netlike pattern of skin discoloration, consider SS as a differential disease, and anti-phospholipid antibody test will be helpful in selecting appropriate drugs for secondary prevention of cerebral infarction.
On-demand oral presentation

O-74  Anterior spinal artery occlusion complicating internal trapping for distal vertebral artery dissecting aneurysm

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Background
Endovascular internal trapping is widely applied to intracranial dissecting vertebral artery (VA) aneurysms; however, ischemic complications have been regarded as an issue of this treatment strategy. Especially, in cases with lesions distal to the posterior inferior cerebellar artery bifurcation, anterior spinal artery (ASA) occlusion can be a serious complication, although it is less frequently occurred due to the development of collateral blood vessels. In this study, we investigated the relationship between the anatomy and ischemic complications of the ASA.

Methods
Fifteen patients with distal VA dissecting aneurysm who underwent endovascular internal trapping in our department were studied. The ASA was preserved as much as possible, and the parent artery was tightly embolized with coils from the dilatated portion to the normal vessel. The anatomy of the ASA origin, ASA occlusion and ischemic complications were analyzed.

Results
ASA branched from the bilateral VA in 4 of 15 cases (27%), from the ipsilateral VA in 3 cases (20%), and from the contralateral VA in 8 cases (53%). ASA occlusion was observed in two cases (13%). In one case, ischemic complication was not occurred due to the collateral flow from the ASA originated from the contralateral side. However, the other patient suffered from a medullary cervical infarction 5 hours after the treatment, even though ASA was preserved during the intervention.

Conclusions
ASA has rich collateral circulation, and cases with bilateral VA origin have been reported in 60-80% at autopsy. In this study, 27% of cases were bilateral VA origin on DSA, suggesting the presence of undetected ASA. In cases with bilateral VA origin, no ischemic complications were observed even if the unilateral ASA was occluded. However, in cases with an ipsilateral VA origin, there is a risk of serious complication due to medullary cervical infarction, and preservation of ASA is necessary.
On-demand oral presentation

**0-75  Iodine-123-Iomazenil SPECT revealed recovery of neuronal viability in association with improvement of cognitive dysfunction after revascularization in moyamoya disease**

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**Background:**
Recent studies indicate $^{123}$I-iomazenil ($^{123}$I-IMZ) SPECT could demonstrate a neuronal viability. Although cognitive dysfunction has been recognized as an important issue in adult moyamoya disease (MMD), standard neuroradiological methods to define such condition are not established.

**Aim:**
Relationship between cognitive function and $^{123}$I-IMZ SPECT before and after revascularization in MMD was firstly examined.

**Method:**
Fifteen patients whose cerebrovascular reactivities (CVRs) were decreased only on the treatment sides were studied. Cognitive function was examined using mini-mental scale examination (MMSE, cutoff 27) and frontal assessment battery (FAB, cutoff 16) before and 6 months after surgery. $^{123}$I-IMZ and $^{123}$I-iodoamphetamine SPECT with acetazolamide challenge were performed at the same timings. Radioreactivities of $^{123}$I-IMZ SPECT at the regions with decreased CVR were investigated using affected-to-contralateral side ratio (ACR).

**Results:**
Eleven patients showed normal cognitive dysfunction before surgery (MMSE 29.5, FAB 18). In their preoperative $^{123}$I-IMZ SPECT, there were no regions with decreased uptakes (ACR 0.97). The cognitive functions and $^{123}$I-IMZ SPECT were not worsened after surgery (MMSE 29.9, FAB 18, ACR 0.99). By contrast, preoperative images of four patients with cognitive dysfunction (MMSE 23.8, FAB 14) showed decrease of $^{123}$I-IMZ uptakes, and the preoperative ACRs (0.82) were significantly lower than those of the normal group. Cognitive functions and $^{123}$I-IMZ uptakes of these four patients tended to ameliorate after revascularization (MMSE 27.5, FAB 15.5, ACR 0.92).

**Conclusion:**
Cognitive functions of MMD patients were associated with $^{123}$I-IMZ uptakes, and could improve after surgery with recoveries of neuronal viabilities.
On-demand oral presentation

O-76 Neuronal dysfunction and hemodynamic disturbance due to venous congestion in dural arteriovenous fistula revealed by 123I-iomazenil single-photon emission computed tomography

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Objective:
Retrograde leptomeningeal venous drainage (RLVD) of a dural arteriovenous fistula (dAVF) is related to neurological morbidity and unfavorable outcomes. However, the direct damage to cortical neurons by dAVF with RLVD has not been elucidated. 123I-iomazenil (123I-IMZ) single-photon emission computed tomography (SPECT) can reveal cerebral blood flow and cortical neuronal damage in early and late images, respectively. This study aimed to assess the relationship association between cerebral venous congestive encephalopathy caused by dAVF using 123I-IMZ SPECT.

Methods:
Based on the pre- and post-treatment magnetic resonance imaging findings, patients were divided into three groups: normal, edema, and infarction groups. Radioactivities in the early and late images of 123I-IMZ SPECT were investigated using the affected-to-contralateral side asymmetry ratio (ACR).

Results:
None of the patients in the normal group showed any symptoms related to venous congestion. In contrast, all the patients in the edema and infarction groups developed neurological symptoms. The ACR in early images in the edema group was significantly lower than that in the normal group and significantly higher than that in the infarction group. The ACR in the late images of the infarction group was significantly lower than those of the normal and edema groups. After treatment, the neurological signs disappeared in the edema group, but only partial improvement was observed in the infarction group. The ACR in early images significantly improved after treatment in the edema group; however, that in late images did not change in any groups.

Conclusions:
123I-IMZ SPECT is useful for evaluating hemodynamic disturbances and neuronal damage in dAVFs. The reduction in early images was correlated with the severity of venous congestive encephalopathy, and the significant reduction in late images is a reliable indicator of irreversible venous infarction caused by RLVD.
On-demand oral presentation

O-77  NOTCH3 p.R75P mutation attributable to hemorrhagic phenotypes in CADASIL

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Background: The prevalence of intracerebral hemorrhage (ICH) and cerebral microbleeds (CMB) among CADASIL patients is higher in East Asian than White people, suggesting genetic factors underlie such hemorrhagic phenotypes. Hence, we evaluated the genotype-phenotype correlation in CADASIL, focusing on the hemorrhagic phenotypes of NOTCH3 p.R75P mutation, the most frequent cysteine-sparing mutation in Japan.

Methods: We retrospectively enrolled consecutive Japanese CADASIL patients in the NCVC CADASIL Registry. Patients who did not undergo 3.0-tesla head MRI were excluded. We investigated whether hemorrhagic phenotypes including symptomatic ICH and multiple CMB —defined as a total CMB of 6 or more on T2*-weighted gradient echo MRI—were associated with the NOTCH3 p.R75P mutation. Quasi-Poisson regression models were used for the analysis.

Results: Among 47 patients with CADASIL (median age, 56 years; male, 53%), the NOTCH3 p.R75P mutation was detected in 13 patients (median age, 55 years; male, 54%) and other NOTCH3 mutations in the remaining 34 patients (median age, 57 years; male, 53%). The prevalence of symptomatic ICH was significantly higher in patients with the NOTCH3 p.R75P mutation compared to those with other NOTCH3 mutations (31% vs. 3%, \(P=0.017\), and the correlation remained significant after adjusting for age, sex, and hypertension (adjusted relative risk [aRR], 6.99 [95% CI, 1.46–53.96]; \(P=0.028\)). The same was true for multiple CMB: the prevalence was higher in those with the NOTCH3 p.R75P mutation than those with other mutations (69% vs. 15%, \(P=0.001\), and aRR [95% CI] was 4.76 [1.65–14.54] (\(P=0.005\)).

Conclusions: The NOTCH3 p.R75P mutation was correlated with hemorrhagic phenotypes including ICH and multiple CMB, suggesting this East Asia-specific NOTCH3 mutation attributable to hemorrhagic CADASIL.
On-demand oral presentation

0-78  The results of surgical therapy for carotid artery stenosis in Nagasaki university

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Carotid artery stenosis is an important cause of stroke and transient ischemic attack. Correctly and rapidly selecting treatment method is essential for the patients with carotid artery stenosis. We retrospectively reviewed our clinical experience of carotid endarterectomy (CEA) and carotid artery stenting (CAS) from April 2017 to December 2021. A total of 91 patients were included in this study, 91 patients underwent CEA and 18 patients underwent CAS. According to our institutional protocol, CAS was selected only for the CEA high-risk group. The patient's background including age, sex, hypertension, dyslipidemia, symptomatic/asymptomatic, degree of stenosis were similar in both groups. Plaque MRI showed T1WI hyper-intensity was 64.8% in CEA group and 50% in CAS group. T1WI hyperintensity was a high risk of postoperative hyper intense spots in diffusion weighted imaging in CAS as well as CEA. Our CEA first-line treatment for carotid artery stenosis seems to be appropriate. Preoperative radiological evaluation including plaque MRI is crucial for both treatments for carotid artery stenosis.
On-demand oral presentation

0-79  Cite Share
Drag-out technique using a large balloon fixed with an aspiration catheter for retrieving residual thrombus on the wall of the superior sagittal sinus

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Objectives: The authors report a patient with sagittal sinus thrombosis that was resistant to reported endovascular treatments but successfully recanalized by dragging out the thrombus using a large balloon fixed with an aspiration catheter.

Case presentation: A 57-year-old man presented with the persistent headache and a simple partial seizure. Diagnostic study with computed tomography and angiography demonstrated the superior sagittal sinus (SSS) thrombosis. Due to the neurological worsening even after systemic heparinization, the patient underwent mechanical thrombectomy. Despite six passes of stent retrievers and a large-bore aspiration catheter, functional recanalization was not achieved. Therefore, the so-called dental floss technique was attempted using a large compliant balloon catheter (Transform 7x7mm). However, the balloon catheter just wobbled along the lesion without recanalization (Fig. A). In order to restrict the movement of the balloon catheter, the distal shaft of the balloon catheter was fixed with the aspiration catheter, and both the balloon and the aspiration catheter were slowly pulled to drag the thrombus out (Fig. B), resulting in recanalization of cortical veins as well as the SSS (Fig. C and D). Fig. E shows large amount of thrombus removed from the SSS (Fig. E). Magnetic resonance venography demonstrated the patent SSS (Fig. F).

Conclusion: Dragging the thrombus using a large balloon fixed with an aspiration catheter was a useful technique to retrieve sticky thrombus in the patients with the sinus thrombosis.
Objective: To evaluate the temporal changes of cerebral perfusion in patients with asymptomatic ipsilateral cerebral artery stenosis during intensive medical treatment, and to determine the correlation between the posttreatment SPECT findings and the initial MR abnormalities.

Methods: This prospective study enrolled 22 patients with asymptomatic ipsilateral cerebral artery stenosis. All underwent two consecutive Tc-99m HMPAO brain SPECT and brain MRI before and after intensive medical treatment at 1-year interval. Demographic variables, underlying medical diseases, the affected side (right vs. left) of involved cerebral artery and the severity of white matter hyperintensities (WMH) on brain MRI were collected. The quantitative analysis was performed to evaluate the mean and total cerebral blood flow (CBF) of both affected and normal cerebral hemisphere by a single blind observer. The CBFs and their change were assessed using Mann Whitney U test.

Results: The mean and total CBFs before treatment showed no differences in both affected and normal hemisphere according to the demographic and clinical variables. After 1-year treatment, the mean and total CBFs were improved in both affected and normal sides. Compared between the group 1 (patients with no or slight degree of WMH) and the group 2 (patients with moderate or severe degree of WMH), the mean and total CBFs in group 1 showed no or slight improvement in both affected and normal side, and the changes of CBFs were insignificant. However, the mean and total CBFs in group 2 showed marked improvement in both affected (p=0.019) and normal side (p=0.066).

Conclusion: Cerebral perfusion of patients with asymptomatic ipsilateral cerebral artery stenosis was improved in both affected and normal cerebral hemisphere after 1-year intensive medical therapy. Improvement of cerebral perfusion after intensive medical therapy was more marked in patients with high WMH on the initial MRI.