Current management of acute ischemic stroke in comprehensive stroke center in Japan

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Background: To show the current management of acute ischemic stroke (AIS) treatment in Japan, and present multicenter prospective registry of large vessel AIS (RESCUE-Japan Registry 2).

Methods: 1) At the approval of landmark device, Japanese government recommend to medical societies to establish guideline (GL) for new treatment. 2) RESCUE registry covered all the patients with acute large vessel occlusion, admitted to the participating hospitals within 24-hours after onset. Factors related to treatment selection and the methods and clinical outcome were analyzed. RESCUE2 have been conducted after stent retrievers approved in Japan.

Results: 1) JSNET established GL for mechanical thrombectomy device in 2010, revised 2014, 2015 and 2018 with JNS and JSS. In this GL, mechanical thrombectomy using stent-retriever is recommended treatment. 2) A total of 2,433 patients registered, 1,003 patients were treated by endovascular treatment (EVT). Among them, only 247 patients (24.6%) matched AHA recommendation. In the low ASPECTS (<5) group, EVT was performed in 146/430 (34%) and favorable outcome (mRS 0-2) was obtained in 24%. In low NIHSS (<5) group, EVT was performed in 46/224 (20%), and favorable outcome was in 76% of EVT group. EVT was performed in 157/424 (37%) of the patients who arrived over 6 hours after onset and favorable outcome was obtained in 38%.

Discussion and conclusions: EVT for AIS have been done by neuro-interventionist in Japan and rapidly growing. EVT was aggressively performed for outside of clinical evidence. Further analysis is necessary with the larger data of nation wide registry.
Early successful reperfusion has been correlated with favorable outcome for acute ischemic stroke with large artery occlusion. Recently our institute switch IA mechanical thrombectomy technique for larger vessel occlusion to Aspiration-Retriever Technique for Stroke (ARTS) based on combined flexible large lumen distal access catheter (Sofia™) and partially resheathed stent retriever. There were 44 patients during last 13 months (between June 2017 and June 2018). The sites of occlusion at the time of angiography included the ICA (n=11), M1 (n=25), and vertebra-basilar artery (n=8). Successful recanalization was achieved in 43 patients (97.7%). We want to describe our new technical strategy for IA mechanical thrombectomy and review it’s efficacy.
Endovascular recanalization for emergent large vessel occlusion

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Endovascular recanalization for internal carotid artery and proximal middle cerebral artery within 6 to 8 hours from the onset without large ischemic core is highly effective treatment with clinical evidences. To shorten the time to recanalization is strongly recommended. In-hospital time saving with work-flow modification is establishing, but pre-hospital time saving has not yet achieved. It is not clear whether mother ship or drip and ship is better in rural area. Octogenarian has also benefit of endovascular recanalization, but it is marginal and most of them wouldn’t be independent. DAWN and DEFFUSE 3 trials revealed the benefits of endovascular recanalization beyond 6 hours using automatic mismatch analyzer call RAPID system. It is not yet established how to introduce this widen therapeutic time window without RAPID system that is not available Japan. There are many uncertain issues such as low ASPECTS with early arrival, basilar artery occlusion or distal middle cerebral artery occlusion. Those patients would have benefits of endovascular recanalization. Recanalization rate of intravenous TPA for large vessel occlusion is very low, then intravenous TPA prior to endovascular recanalization is debatable. To clarify We had started multicenter prospective randomized trial comparing endovascular recanalization with or without TPA for the patients with internal carotid or M1 occlusion within 8 hours from the onset.
The effectiveness of intra-arterial thrombectomy (IAT) protocol for decreasing door-to-recanalization time duration in acute major arterial occlusion

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Introduction: Intra-arterial thrombectomy (IAT) is safe and effective treatment modality in acute major arterial occlusion. Among the most important factors associated with good prognosis, there are early and successful recanalization. However, because of several cause, it was not well-determined to set IAT protocol to decrease time duration during door-to-recanalization in each institute. The aim of this study is to investigate the effectiveness of IAT protocol for decreasing door-to-recanalization time duration.

Material & Methods: We examined and reported three time duration (min): door-to-angioroom, angioroom-to-puncture, and puncture-to-recanalization. According to each three steps, we made set-up IAT protocol. And we compared time duration between patients not applied to IAT protocol (Mar 2011 - Feb 2014) and patients applied to IAT protocol (Mar 2014 - Jul 2018).

Results: 294 patients who underwent IAT in anterior circulation were included in this study. There are 59 patients who were not applied to IAT protocol and 235 patients who were applied to IAT protocol. In three steps, there were significant time reduction in the patient treated before and after IAT protocol.

Conclusion: Application of a IAT protocol showed a significant time reduction for faster recanalization in patients with acute major arterial occlusion. We suggest that better IAT protocol according to each step on door-to-angioroom, angioroom-to-puncture, and puncture-to-recanalization can be needed to decrease time duration in recanalization therapy.
Background and Purpose: The role of telemedicine in the stroke team became important for rapid management of stroke patient workflow. We developed a cloud based telestroke management app, “JOIN” for stroke management.

Methods: A system was created on the basis of communicating patient data and images between hospital systems and participating staff members in and out of the hospital through their standard, using smartphone. The system is able to transfer clinical data, CT, MR, angiographic, intraoperative images, and expert opinion in real time. JOIN has key functions that may improve the care of stroke patients, including the ability to: (1) exchange information such as patient data and medical images in real time throughout the entire process of patient management, (2) track each step of the protocol from door to discharge, and (3) facilitate real-time interaction of all team members via text, audio and a video chat system.

Results: The system showed successful information transfer, allowing medical staff to discuss patients’ diagnosis and management using a system.

Conclusions: We report our Cloud based telestroke system “JOIN” for acute patient management of ischemic stroke patients.
Endovascular thrombectomy for acute ischemic stroke; DEFUSE the time barrier with the DAWN of image based selection criteria

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“That’s one small step for a man, one giant leap for mankind.”
(Neil Armstrong : July 20, 1969)

1. One step
An avalanche of many randomized controlled trials focusing mechanical thrombectomy in acute ischemic stroke due to acute proximal large vessel occlusion (LVO) presenting within 6 h of the onset symptoms have opened new era of acute ischemic stroke treatment. A pooled analysis of these trials confirmed the efficacy of thrombectomy that is performed within 6 hours after the onset of stroke in patients with occlusion of a cerebral large vessel (intracranial internal carotid artery or proximal middle cerebral artery).

2. Giant leap
1) The DAWN (DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention with Trevo) trial\(^1\) investigated the efficacy and safety of endovascular thrombectomy that is performed 6 to 24 hours after the onset of stroke. The DAWN trial were selected specifically because they had a region of brain that was poorly perfused but not yet infarcted. In essence, the usual 6-hour time window for stroke treatment was replaced with a “tissue window.”

2) The DEFUSE-3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke-3) trial\(^2\) investigated the use of mechanical thrombectomy in ischemic stroke patients 6 to 16 after the onset of symptoms. The results of the DEFUSE-3 trial are complementary to the results of the DAWN trial. Based on these differences 40% of the patients in DEFUSE-3 trials would not have met the inclusion criteria of the DAWN trial but still showed improved outcomes in the thrombectomy arm. A single comprehensive stroke study showed that 1.7% of patients qualified for DAWN clinical trial enrollment with an additional 0.6% to 1% qualifying for the DEFUSE-3 trial\(^3\).

Further research on advanced imaging based approaches to select appropriate patients, may widen the time-window for patient selection and would contribute immensely to early thrombolytic strategies, better recanalization rates, and improved clinical outcomes.

For these recent trials of thrombectomy beyond 6 hours, 2 different types of mismatch have been defined\(^4\):
1. TMM:
- maximal volume of the ischemic core, and
- the ratio and the absolute difference critically hypoperfused region volume outlined by a TMax delay >6 s.

2. Clinical infarct mismatch:
- maximal volume of the ischemic core, and
- neurological deficit assessed by the National Institutes of Health Stroke Scale.

In conclusion, Patients experiencing an acute IS within 6 to 24 hours of last known normal with a demonstrable internal carotid artery/M1 occlusion and a clinical infarct mismatch based on DAWN criteria (up to 24 hours) or a TMM based on DEFUSE-3 criteria (up to 16 hours) should be treated with thrombectomy. 4)

3. Derivatives
1) The ASTER (contact aspiration vs stent retriever for successful revascularization) study revealed that first-line thrombectomy with contact aspiration compared with stent retriever did not result in an increased successful revascularization rate5).

2) The WAKE-UP (Efficacy and safety of MRI-based thrombolysis in wake-up stroke) trial revealed that in patients with acute stroke with an unknown time of onset, intravenous alteplase guided by a mismatch between diffusion-weighted imaging and FLAIR in the region of ischemia resulted in a significantly better functional outcome and numerically more ICHs than placebo at 90 days6). The primary investigator said that “It will make a big impact on clinical practice as about 25% of stroke patients have undetermined time of onset, and approximately one third to one half of these will now qualify for the treatment based on these imaging criteria.” 7)

3) Distal intracranial occlusions can be treated safely and successfully with endovascular therapy. These results need to be corroborated by larger prospective controlled studies8).

4) Direct transfer and telemedicine-based decision will widen inclusion criteria 9).

References


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Regional project for the purpose of training interventionists of thrombectomy and making homogeneous performance - Aichi model -

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[Purpose] Demands of thrombectomy for cerebral embolism rapidly increased since its efficacy was recognized. National guideline addresses the importance of training the qualified interventionists and of the systematic establishment of comprehensive stroke center. We launched new project to improve the quality of the treatment for acute stroke under the collaboration of four universities in Aichi prefecture and thanks to the support of Japanese stroke association and prefectural government.

[Methods] We asked the questionnaire about the actual situation of acute stroke care to 140 institutes in the prefecture. Contents included annual numbers of stroke patients and treatment methods, the circumstance (equipment and staff) and the problem on stoke management. Then, we produced the seminar containing lectures of basic knowledge of pathophysiology of ischemia and know-how of thrombectomy as well as hands-on training using vascular or simulation model for all available devices. Announcement of the seminar was sent to institutes in the prefecture particularly to the depopulated area for thrombectomy. We also issued a special textbook to facilitate understanding of trainees.

[Results and Discussion] Responses to questionnaire were obtained from 115 institutes (a response rate: 82%). Thrombectomy was performed in 432 patients in 31 instituted within 2017, which means about 15% of cerebral embolism patients. The rate of the implementation of thrombectomy was higher in urban areas, however it was very low in rural sides, less than 10 % of urban rate. The seminar was performed the whole day with 141 participants including 40 hands-on trainees. Most participants impressed the practices were very fruitful, but requested more time to round each hands-on section. Based on the results we plan to back-up the trainees who encounter acute stroke patients because they do not yet have sufficient skills for the clinical cases even though they completed the seminar.

[Conclusion] The project to train the interventionists of thrombectomy should be established in each region because the backgrounds are quite different. To take it easier the collaboration between government, association, departments concern in universities and real clinicians in big stroke centers is essential.