

2020 Guideline for Prehospital Management, Emergency **Evaluation and Treatment of Patients With Acute** Ischemic Stroke: A Guideline for Healthcare Professionals from the Taiwan Society of Emergency Medicine and **Taiwan Stroke Society**

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To improve the clinical outcomes of patients with acute ischemic stroke, the public, pre-hospital care system, and hospitals should cooperate to achieve quick assessment and management for such patients and to start treatment as soon as possible. To reach the goal, the Consensus Group, including emergency physicians and neurologists in the Taiwan Society of Emergency Medicine and Taiwan Stroke Society, performed an updated review and discussion for the local guidelines. The guidelines consist of 12 parts, including public education program, evaluation and management in the emergency medical system, emergency medical system, assessment of stroke care capability of the hospital by independent parties, stroke team of the hospital, telemedicine, organization, and multifaceted integration, improvement of quality of care process of stroke system, initial clinical and imaging evaluations after arriving at the hospital, imaging evaluation for indications of intravenous thrombolysis, imaging evaluation for indications of endovascular thrombectomy, and other

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diagnostics. For detailed contents in Chinese, please refer to the Taiwan Stroke Society Guideline and Taiwan Emergency Medicine Bulletin.

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Introduction

In 1995, a clinical trial conducted by the National Institute of Neurological Disorders and Stroke found that administering recombinant tissue-type plasminogen activator to patients with acute ischemic stroke (AIS) within 3 hours of stroke onset can significantly improve favorable outcome after 3 months. Since then, AIS treatment has entered a new era. In 2008, one European multicenter clinical trial further showed that intravenous thrombolysis (IVT) administered 3.0-4.5 hours after stroke onset could still improve the probability of favorable outcomes.² The Taiwan Stroke Society revised the IVT treatment guidelines in 2008, 2013, and 2019 in accordance with the research evidence and the trend of changes in international standards.³ The recovery of the patient's neurological functions is significantly associated with the timing of starting IVT treatment, as illustrated by two meta-analyses that the shorter the time interval between the onset of stroke symptoms and IVT, the greater the odds of 3-month favorable functional outcomes. 4,5 Therefore, minimizing the time-lapse from the onset of stroke to IVT treatment is vital.

In 2015, five pivotal endovascular thrombectomy (EVT) trials, including MR CLEAN, EXTEND IA, ESCAPE, SWIFT PRIME, and REVASCAT, 6-10 demonstrated that the clinical outcomes of AIS patients with large vessel occlusion (LVO) were significantly improved by IVT combined with EVT, compared with IVT alone. Later in the same year, the American Heart Association (AHA) strongly recommended the consideration of EVT in addition to IVT in eligible stroke patients with LVO. 11 Therefore, EVT has become the international standard of care for AIS patients with LVO. 12 In consistence with IVT, the timing of EVT with corresponding reperfusion also affects the patient's prognosis.

Appropriate pre-hospital emergency management and systematic care offering to AIS patients might increase the number of patients receiving IVT and EVT, and shortened the time from the onset of symptoms to treatment. This guideline adopts the Class of Recommendation (COR) (graded as Class I, IIa, IIb, III) and Level of Evidence (LOE) (graded as A, B-R, B-NR, C-LD, and C-EO) according to AHA/ ACC (American College of Cardiology)/HRS (Heart Rhythm Society) as shown below.¹³ For detailed contents in Chinese, please refer to the Taiwan Stroke Society Guideline and Taiwan Emergency Medicine Bulletin.

Public Education Program

Recommendations

- 1. Government agencies shall work with relevant medical societies and professionals to implement public education programs, which emphasize stroke symptoms and the need to seek immediate medical attention (for example, dial 119). These education programs shall cover different geographical regions (including outlying islands and rural areas), ethnic groups, age, and gender. (COR I, LOE B-NR)
- 2. The public education programs shall be individually designed for the public, physicians, other healthcare providers, emergency medical personnel, and other subjects of different nature to increase the proportion of stroke literacy and the usage of the emergency medical system. (COR I, LOE C-EO)
- 3. When a suspected stroke occurs, it is recommended that the patient or his/her surrounding persons dials 119 immediately to activate the emergency medical system and dispatching an ambulance to send the patient to the hospital as soon as possible. (COR I, LOE B-NR)

Evaluation and Management in Emergency Medical System

Recommendations

1. The on-scene first-aid providers and emergency

Hsieh et al.

- medical system dispatcher are recommended to recognize stroke patients using stroke assessment tools, and the emergency medical system dispatcher shall dispatch an ambulance to the scene as the highest priority. (COR I, LOE B-NR)
- 2. The emergency medical personnel are recommended to notify the receiving hospital that a suspected stroke patient is en route so that the hospital can initiate relevant measures and resources before the patient arrives. (COR I, LOE B-NR)

Emergency Medical System

Recommendations

- Healthcare facilities are recommended to assemble a cross-disciplinary stroke care team according to the Classification on Emergency Medical Capability of the Hospital and divided into (1) healthcare institutions that provide initial care including IVT therapy, and (2) hospitals that provide EVT and comprehensive peri-procedural care. (COR I, LOE A)
- 2. The establishment of stroke triage regulations and standard protocols by central and local government, along with healthcare authorities (i.e., the Department of Medical Affairs and the fire departments of different counties and cities), relevant medical societies and professionals, is recommended to ensure rapid recognition and evaluation of stroke patients with the usage of effective stroke indicators. (COR I, LOE B-NR)
- 3. Patients with suspected acute stroke shall be transported to a hospital that can provide IVT treatment as soon as possible, and the eligibility of the subsequent EVT treatment shall be also evaluated. (COR I, LOE B-NR)

Assessment of the Stroke Care Capability of the Hospital by Independent Parties

Recommendation

It is recommended that independent parties (such as Joint Commission of Taiwan and Department of Medical Affairs) may evaluate the quality of stroke treatment in the healthcare facilities according to the Classification on Emergency Medical Capability of the Hospital and relevant regulations. (COR I, LOE B-NR)

Stroke Team of the Hospital

Recommendations

- 1. Establish an acute stroke team consisting of physicians, nurses, case managers, radiology and laboratory personnel, and an organized in-hospital standard protocol to urgently evaluate patients with a suspected stroke. Stroke patients shall be subjected to a careful clinical assessment, including neurological examination and National Institutes of Health Stroke Scale (NIHSS) assessment. (COR I, LOE B-NR)
- 2. Implement multicomponent quality improvement actions, including emergency department education and establishment of an inter-departmental team with neurological expertise, to improve the quality and quantity of IVT therapy. (COR I, LOE A)
- 3. Establish and monitor the goal of door-to-needle time for IVT administration (the recommended goal is within 60 minutes). (COR I, LOE B-NR)

Telemedicine

Recommendations

- 1. For areas lacking radiological experts, it is recommended to use the teleradiology system approved by the healthcare authorities to provide real-time brain imaging interpretation services for patients with acute stroke suspicion. (COR I, LOE A)
- 2. Telemedicine can be implemented according to the regulations of the Ministry of Health and Welfare and after the approval of the healthcare authorities, and shall be supported by each member of the medical team. (COR I, LOE C-O)
- 3. Telemedicine and teleradiology interpretation of acute stroke patients can improve the accuracy of the decision-making of IVT therapy and guide inter-hospital transfer for EVT. (COR IIa, LOE B-R)

Organization and Multifaceted Integration

Recommendations

- 1. Standard protocols and procedures of inter-hospital transferal shall be established to ensure safe and effective care for stroke patients. (COR I, LOE C-EO)
- 2. EVT shall be conducted in the healthcare facilities certified by the Accreditation of Emergent Medical Ability of the Hospital, including rapid executions

- of cerebral angiography, certified neurointerventional specialists, and a comprehensive peri-procedural care team. (COR I, LOE C-EO)
- 3. Healthcare institutions that provide initial care (including IVT therapy) may consider developing an examination procedure that can perform emergent and noninvasive intracranial angiography to determine patients who are suitable for transferring for an evaluation and treatment of EVT. This procedure may be helpful in shortening the time to EVT. (COR IIb, LOE C-LD)
- 4. Government agencies and insurance institutions shall implement appropriate reimbursement regulations for the care and professional expenses needed for acute stroke patients to achieve an ideal outcome. (COR I, LOE C-EO)

Improvement of Quality of Care Process of Stroke System

Recommendation

Healthcare institutions shall organize a cross-disciplinary quality improvement committee to review and monitor the quality benchmarks, indicators, evidence-based implementation of stroke care, and patient outcomes, which will help improve the quality of care. (COR I, LOE B-NR)

Initial Clinical and Imaging Evaluation After Arriving at the Hospital

Recommendations

- 1. The clinical use of a stroke severity scoring scale is recommended, and NIHSS is preferred. (COR I, LOE B-NR)
- 2. All patients with suspected AIS shall receive emergency brain imaging evaluation. (COR I, LOE A)
- 3. Before the patient receives IVT, non-contrast computed tomography (CT) scan of the brain is effective to rule out intracranial hemorrhage. (COR I, LOE A)

Imaging Evaluation for Indications of IVT

Recommendations

1. Since the efficacy of IVT is related to the start time

- of treatment, treatment shall be started as soon as possible for patients with indications and shall not be delayed by performing additional multimodal neuroimaging, such as CT perfusion and magnetic resonance perfusion. (COR I, LOE B-NR)
- 2. For patients with AIS whose stroke symptoms are first noted upon awakening from sleep or have an unknown time of stroke onset but exceeding 4.5 hours from the last time known to be normal, finding an imaging mismatch between diffusion-weighted imaging and fluid-attenuated inversion recovery of magnetic resonance imaging in the region of brain ischemia is helpful for IVT.14 (COR IIa, LOE B-R)
- 3. For patients with AIS whose symptoms occurred between 4.5 and 9.0 hours after stroke onset or those on awakening with stroke (if within 9 hours from the midpoint of sleep), using CT perfusion to identify patients who had hypoperfused but salvageable brain tissue is helpful for patients to receive IVT.15 (COR IIa, LOE B-R)

Imaging Evaluation for Indications of EVT

Recommendations

- 1. For patients who are eligible for EVT, noninvasive intracranial arterial angiography, such as CT angiography or magnetic resonance angiography, shall be performed as the initial imaging evaluation. (COR I, LOE A)
- 2. For patients who are suspected LVO and eligible for EVT and without a history of renal function impairment, it is reasonable to perform CT angiography before obtaining the serum creatinine result. (COR IIa, LOE B-NR)
- 3. For patients who are potentially indicated for EVT, in addition to intracranial vascular examinations, it is reasonable to perform extracranial carotid and cervical vertebral angiography, which can provide useful information on whether the patients are suitable for treatment and endovascular treatment plan. (COR IIa, LOE C-EO)
- 4. It may be reasonable to consider the condition of collateral circulation to determine whether certain patients are suitable for EVT. (COR IIb, LOE
- 5. For patients with LVO in the anterior circulation presenting 6-24 hours from the last time known to

Hsieh et al.

be normal, it is recommended to use CT perfusion imaging or magnetic resonance diffusion-weighted imaging and/or perfusion imaging in assisting the selection of patients suitable for EVT. However, this recommendation is made only if the patients meet the eligibility criteria of either DAWN or DE-FUSE 3 trial. 16,17 (COR I, LOE A)

Other Diagnostics

Recommendations

- 1. For all patients, blood glucose testing must be performed before starting IVT. (COR I, LOE B-NR)
- 2. A baseline electrocardiogram is recommended for patients with AIS, but it shall not delay the start of IVT. (COR I, LOE B-NR)
- 3. A baseline troponin test is recommended for patients with AIS, but it shall not delay the start of IVT or EVT. (COR I, LOE C-LD)
- 4. In the absence of evidence of acute lung, heart, and pulmonary vascular disease, it is uncertain whether a chest X-ray image is useful in the hyperacute phase of the stroke. If this test is performed, it shall not delay the start of IVT. (COR IIb, LOE B-NR)

Conflicts of Interest Statement

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References

- 1. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995;333:1581-1587. doi:10.1056/NEJM199512143332401
- 2. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med 2008;359:1317-1329. doi:10.1056/NEJMoa0804656
- 3. Chen CH, Hsieh HC, Sung SF, et al. 2019 Taiwan Stroke Society Guideline for intravenous thrombolysis in acute ischemic stroke patients. Formos J Stroke 2019;1:1-22. doi:10.6318/FJS.201906_1(1).0001
- Hacke W, Donnan G, Fieschi C, et al. Association of outcome with early stroke treatment: pooled analysis of AT-LANTIS, ECASS, and NINDS rt-PA stroke trials. Lancet 2004;363:768-774. doi:10.1016/S0140-6736(04)15692-4

- 5. Lees KR, Bluhmki E, von Kummer R, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. Lancet 2010;375:1695-1703. doi:10.1016/S0140-6736(10)60491-6
- Berkhemer OA, Fransen PSS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015;372:11-20. doi:10.1056/NEJ-Moa1411587
- Campbell BCV, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 2015;372:1009-1018. doi:10.1056/ NEJMoa1414792
- 8. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 2015;372:1019-1030. doi:10.1056/ NEJMoa1414905
- Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med 2015;372:2285-2295. doi:10.1056/NEJ-
- 10. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 2015;372:2296-2306. doi:10.1056/NEJ-Moa1503780
- 11. Powers WJ, Derdeyn CP, Biller J, et al. 2015 American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2015;46:3020-3035. doi:10.1161/ STR.0000000000000074
- 12. Tang SC, Tsai LK, Chen CJ, et al. 2019 Taiwan stroke society guideline for endovascular thrombectomy in acute ischemic stroke patients. Formos J Stroke 2019;1:77-89. doi:10.6318/FJS.201909_1(2).0001
- 13. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 Update to the 2018 Guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2019;50:e344-e418. doi:10.1161/STR.0000000000000211
- 14. Thomalla G, Simonsen CZ, Boutitie F, et al; WAKE-UP Investigators. MRI-guided thrombolysis for stroke with unknown time of onset. N Engl J Med 2018;379:611-622. doi:10.1056/NEJMoa1804355
- 15. Ma H, Campbell BCV, Parsons MW, et al. Thrombolysis guided by perfusion imaging up to 9 hours after onset of stroke. N Engl J Med 2019;380:1795-1803. doi:10.1056/

NEJMoa1813046

16. Nogueira RG, Jadhav AP, Haussen DC, et al; DAWN Trial Investigators. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl JMed 2018;378:11-21. doi:10.1056/NEJMoa1706442

17. Albers GW, Marks MP, Kemp S, et al; DEFUSE 3 Investigators. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. N Engl J Med 2018;378:708-718. doi:10.1056/NEJMoa1713973