

**Supplementary Methods 1.** Criteria for IV rtPA therapy by National Health Insurance in Taiwan.

Inclusion criteria:

1. Age between 18 and 80 years old
2. Non-contrast computed tomography (CT) scan showing no hemorrhage
3. Acute ischemic stroke with symptoms onset less than 3 hours and complete evaluation

Exclusion criteria:

1. Acute ischemic stroke with symptoms onset more than 3 hours or unknown
2. Rapid improvement of stroke symptoms or stroke severity too mild (the National Institutes of Health Stroke Scale [NIHSS] less than 6)
3. Stroke severity too severe (NIHSS greater than 25) or hypodensity greater than 1/3 cerebral hemisphere on CT findings
4. Seizure at onset
5. Recent head trauma, or stroke (less than 3 months)
6. History of stroke with Diabetes mellitus
7. Heparin used in 48 hours before stroke and prolonged aPTT
8. Platelets less than 100,000/mm<sup>3</sup>
9. Active internal bleeding
10. Intracranial brain tumor or brain aneurysm or vascular malformation
11. Systolic blood pressure greater than 185 or diastolic blood pressure greater than 110 mm Hg or needed to be aggressively treated by IV medication to reach these target levels
12. Glucose less than 50 or greater than 400 mg/dL
13. Patients currently receiving oral anticoagulant, such as Warfarin sodium with PT INR>1.3
14. History of intracranial hemorrhage or brain aneurysm or vascular malformation or brain tumor, intracranial or spinal surgery
15. History, suspicion or approval of intracranial hemorrhage, subarachnoid hemorrhage
16. Serious and uncontrolled hypertension
17. Recent surgery, serious trauma or head injury (less than 10 days) including acute myocardia infarct
18. Prolonged or traumatic cardiopulmonary cerebral resuscitation (more than 2 minutes), delivery, recent (less than 10 days) uncompressible vascular puncture (such as subclavian or neck central venous puncture)
19. Severe hepatic diseases, including hepatic failure, liver cirrhosis, portal hypertension (esophageal varicose vein), and acute hepatitis
20. Hemorrhagic retinopathy (such as diabetic), or other hemorrhagic ophthalmic conditions
21. Subacute bacterial endocarditis, acute pericarditis
22. Acute pancreatitis
23. Peptic ulcer disease in recent 3 months
24. Aneurysm, arteriovenous malformation
25. Tumor with easy bleeding
26. Allergy to rt-PA or adjuvant agent
27. Other conditions with increased risk of bleeding, such as hemodialysis, heart failure, cachexia