**Table 2. Stroke Features and Process Measures for the 600 Patients**

| Stroke Features | |
|---|---|
| Time of stroke onset | |
| 6 AM to 2 PM | 292 (48.7%) |
| 2 PM to 10 PM | 244 (40.7%) |
| 10 PM to 6 AM | 64 (10.6%) |
| Arterial occlusion site (n=546) | |
| Internal carotid artery | 91 (16.7%) |
| Middle cerebral artery trunk (M1) | 159 (29.1%) |
| Middle cerebral artery branch (M2) | 108 (19.8%) |
| Anterior cerebral artery | 7 (1.3%) |
| Posterior cerebral artery | 18 (3.3%) |
| Vertebral artery | 4 (0.7%) |
| Basilar artery | 22 (4.0%) |
| Stroke subtype | |
| Cardioembolism | 380 (63.3%) |
| Atherothrombotic stroke | 91 (15.2%) |
| Lacune | 29 (4.8%) |
| Other mechanisms | 100 (16.7%) |
| ASPECTS on CT (n=501) | 10 (8–10) |
| ASPECTS on DWI (n=520) | 8 (7–10) |
| Initial NIHSS score | 13 (7.3–19) |
| Process measure | |
| Onset-to-treatment time, minutes | 145 (121–166) |
| Interruption of rtPA | 6 (1.0%) |
| IV antihypertensives just before rtPA | 164 (27.6%) |
| IV edaravone | 502 (83.7%) |

Data are no. of patients (%) and median (interquartile range) for discontinuous variables.

patients, 422 (70.3%) met the criteria of the European license (patients ≤80 years old with an initial NIHSS score ≤24 and without any history of prior stroke and concomitant diabetes).

The baseline characteristics of the 600 patients as well as their stroke features and process measures are listed in Tables 1 and 2. The leading risk factor was hypertension (61.0%) followed by atrial fibrillation (43.4%). MR angiography was performed in 479 patients, CT angiography was performed in 15, and ultrasound was performed in 369. The leading site of arterial occlusion was the trunk of the middle cerebral artery (29.1%) followed by its branch (19.8%). The leading stroke subtype was cardioembolism (63.3%).

The median NIHSS score decreased from 13 (interquartile range, 7.25 to 19) before rtPA to 8 (interquartile range, 3 to 16) 24 hours later. ICH developed in 119 patients (19.8%; 16.8% to 23.2%); of these, 30 showed parenchymal hemorrhage Type I (5.0%) and 21 showed parenchymal hemorrhage Type II (3.5%). Symptomatic ICH within 36 hours developed in 23 patients (3.8%; 2.6% to 5.7%). Symptomatic ICH within 36 hours per the SITS-MOST definition developed in 8 patients (1.3%; 0.7% to 2.6%); 7 of these met the criteria of the European license (7 of 422 [1.7%; 0.8% to 3.4%]).

Vital prognosis at 3 months was available for all 600 patients, but the mRS scores for 5 patients were not available. mRS scores at hospital discharge in these 5 patients were 2, 4, 4, 5, and 5, and their durations of hospitalization were 38, 30, 33, 18, and 37 days, respectively.

Of the total 600 patients, 199 patients (33.2%; 95% CI, 29.5% to 37.0%) had an mRS score ≤1 at 3 months, when the score at hospital discharge was used for 5 patients who were lost to follow-up at 3 months (Figure). When 65 patients with a premorbid mRS score ≥2 were excluded from the analysis, 199 (37.2%; 33.2% to 41.4%) of 535 patients had an mRS score ≤1. In addition, when patients who did not meet the criteria of the European license were excluded, 162 (40.6%; 35.9% to 45.5%) of 399 patients had a score ≤1.

At 3 months, 43 patients (7.2%; 95% CI, 5.4% to 9.5%) died, including 7 with symptomatic ICH. Nineteen patients died within the initial week of stroke. Fifteen patients died directly of stroke, 7 died of heart disease (5 heart failure, one heart rupture, and one infective endocarditis) and 6 died of pneumonia. Of 422 patients who met the criteria of the European license, 20 died (4.7%; 3.1% to 7.2%).

Multivariate regression analysis using a backward selection method indicated that younger age, lower initial NIHSS

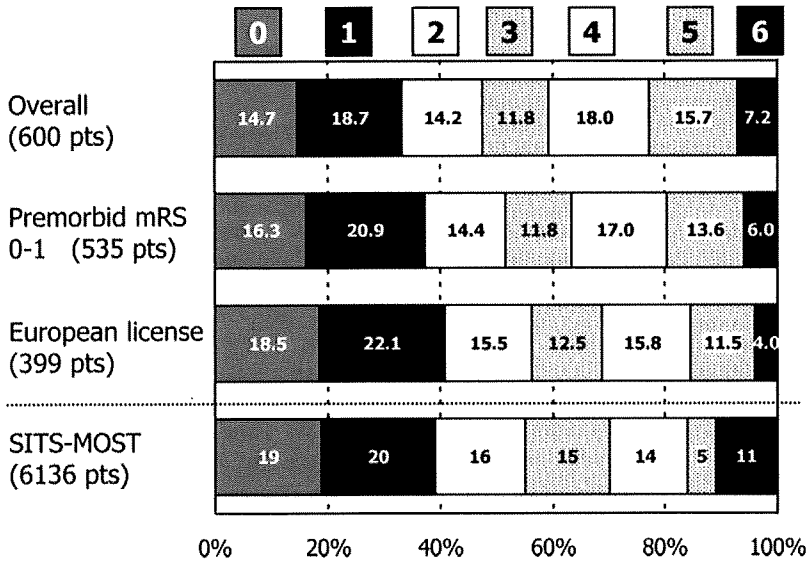


**Figure.** mRS score at 3 months in the present patients and those in SITS-MOST.

**Table 3. Characteristics Associated With an mRS Score ≤1 and Death at 3 Months**

| Characteristic | OR | 95% CI | *P* Value |
|---|---|---|---|
| mRS score ≤1 | | | |
| Age, per 10-year increase | 0.74 | 0.59–0.91 | 0.006 |
| Initial NIHSS score, per 1-point increase | 0.92 | 0.88–0.95 | <0.001 |
| Glucose, per 1-mmol/L increase | 0.90 | 0.81–1.00 | 0.053 |
| Internal carotid artery occlusion | 0.27 | 0.11–0.61 | 0.003 |
| ASPECTS on CT, per 1-point increase | 1.25 | 1.06–1.51 | 0.013 |
| IV antihypertensives just before rtPA | 0.38 | 0.21–0.67 | 0.001 |
| Death | | | |
| Congestive heart failure | 5.90 | 2.74–12.27 | <0.001 |
| Prior use of statin | 1.59 | 0.60–3.72 | 0.331 |
| Glucose, per 1-mmol/L increase | 1.14 | 1.03–1.26 | 0.015 |

Adjusted by characteristics selected by a backward selection procedure. "mRS score ≤1" was analyzed based on 535 patients with a premorbid mRS ≤1. "Death" was analyzed based on 600 patients.

score, absence of ICA occlusion, higher ASPECTS on CT, and absence of IV antihypertensives just before rtPA were independently related to an mRS ≤1 at 3 months (Table 3). In addition, hypertension ($P$=0.013), higher initial systolic blood pressure ($P$=0.046), and higher initial glucose level ($P$=0.034) were inversely related, and cardioembolism ($P$=0.034) was positively related to an mRS ≤1 after simple adjustment for sex, age, and the initial NIHSS score.

After multivariate regression analysis using a backward selection method, congestive heart failure and higher initial glucose level were independently related to death at 3 months (Table 3). In addition, older age ($P$=0.048), higher initial NIHSS score ($P$<0.001), ischemic heart disease ($P$<0.001), prior use of anticoagulants ($P$=0.047), prior use of antihypertensives ($P$=0.016), lower body weight ($P$=0.032), and ICA occlusion ($P$<0.001) were positively related, and use of the IV free radical scavenger, edaravone (which was approved for clinical use in Japan in 2001 after a multicenter randomized clinical trial),[14] was inversely related to death ($P$=0.002) after adjustment for sex, age, and the NIHSS score.

## Discussion

The first major finding of this study was that 33.2% (95% CI, 29.5% to 37.0%) of patients with stroke in our cohort had an mRS ≤1 at 3 months after receiving low-dose (0.6 mg/kg) IV alteplase therapy, a therapeutic strategy that has only been approved in Japan. When patients who did not meet the criteria of the European license as well as those with a premorbid mRS score ≥2 were excluded, like in SITS-MOST,[13] 40.6% (35.9% to 45.5%) had a score ≤1. These percentages were similar to the percentage of patients with an mRS score ≤1 in J-ACT[2] (37%) and those in Western postmarketing surveys using 0.9 mg/kg alteplase (35% in Standard Treatment with Alteplase to Reverse Stroke [STARS]; 37% in Canadian Alteplase for Stroke Effectiveness Study [CASES]; 38.9%, 37.7 to 40.1% in SITS-MOST).[13,15,16] In addition, the frequency of symptomatic ICH in our study (3.8%; 2.6% to 5.7%) was relatively low compared with that in the NINDS study (6.4%)[10] and CASES (4.6%; 3.4% to 6.0%)[16] and similar to that in SITS-MOST (1.3%; 0.7% to 2.6% in ours versus 1.7%; 1.4% to 2.0% in SITS-MOST using the SITS-MOST definition).[13] Our definition for symptomatic ICH was similar to the others; accordingly, this low frequency suggests a true reduction in risk of ICH by low-dose rtPA. Our mortality rate at 3 months (4.7%; 3.1% to 7.2%, for patients meeting the criteria of the European license) was also lower than that in SITS-MOST (11.3%; 10.5% to 12.1%)[13] and CASES (22.3%; 20.0% to 25.0%).[16] Because our result was from experienced centers, it might be better than the overall results in Japan. At the very least, low-dose IV rtPA given to Japanese patients in experienced centers resulted in relatively good efficacy and safety compared with regular-dose therapy in Western patients.

The second major finding was that age, initial neurological severity, ICA occlusion, ASPECTS on CT, and IV antihypertensives just before rtPA were related to long-term independence, and congestive heart failure and initial glucose level were related to mortality after low-dose rtPA; some of these are known predictors.[4–6] Of these, admission hyperglycemia was reported to be associated with a poor recanalization rate of the occluded artery and increased risk of death, symptomatic ICH, and poor functional status.[6,17,18] High acute blood pressure is associated with poor outcome after rtPA.[4,6,7,19] In a multivariate analysis from Safe Implementation of Thrombolysis in Stroke–International Stroke Thrombolysis Register (SITS-ISTR) involving 11 080 patients, a high average systolic blood pressure at 2 to 24 hours was associated with high mortality, high rates of symptomatic ICH, and low rates of functional independence.[7] However, the effect of emergent IV antihypertensives on stroke outcome is being disputed; a recent study found no effect.[20] A major advance in our data set was that we had pretreatment MR angiography information. In addition to our MR angiography studies,[3] some studies using transcranial Doppler showed ICA occlusion to be resistant to IV rtPA.[21,22] We should note that our patients with ICA occlusion had much higher initial median NIHSS scores than those without ICA occlusion (18 versus 12, $P$<0.001), although the inverse association between ICA occlusion and long-term independence was significant after adjustment for the NIHSS score. An association of lower body weight with mortality after adjustment for sex, age, and the NIHSS score suggests that alteplase at a dose of 0.6 mg/kg was insufficient for lightweight patients, because a dose in proportional to body weight may be inadequate in such patients due to the plasma distribution and activation of alteplase.

The limitations of the present study include missing data of 3-month mRS scores for 5 patients as well as missing data for some baseline characteristics; these affected the data on chronic outcomes and limited the number of patients available for the multivariate analyses. Second, this was an observational study, and patient eligibility for rtPA was determined according to each patient's situation, although the determination was principally based on the Japanese guidelines.[9] We did not collect data for patients with stroke who visited our centers within 3 hours after onset and did not receive thrombolysis. Third, some continuous variables might

have been re-evaluated as categorized factors for proper statistical analyses. Our previous studies indicated that ASPECTS on DWI beyond threshold values was indicative of poor stroke outcome,[3,8] but the present study using ASPECTS as a continuous variable did not. Detailed analyses on outcome predictors should be explored in further subanalyses.

In conclusion, chronic outcomes and the factors affecting chronic outcomes were determined in Japanese patients with stroke receiving low-dose IV rtPA therapy. In future studies, we plan to determine the contribution of each risk factor and other patient characteristics to the outcomes.

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## Disclosures

None.

## References

1. Yamaguchi T, Kikuchi H, Hayakawa T; Japanese Thrombolysis Study Group. Clinical efficacy and safety of intravenous tissue plasminogen activator in acute embolic stroke: a randomized, double-blind, dose comparison study of duteplase. In: Yamaguchi T, Mori E, Minematsu K, del Zoppo GJ, eds. *Thrombolytic Therapy in Acute Ischemic Stroke III*. Tokyo: Springer-Verlag; 1995:223–229.
2. Yamaguchi T, Mori E, Minematsu K, Nakagawara J, Hashi K, Saito I, Shinohara Y; Japan Alteplase Clinical Trial (J-ACT) Group. Alteplase at 0.6 mg/kg for acute ischemic stroke within 3 hours of onset: Japan Alteprase Clinical Trial. *Stroke*. 2006;37:1810–1815.
3. Nakashima T, Toyoda K, Koga M, Matsuoka H, Nagatsuka K, Takada T, Naritomi H, Minematsu K. Arterial occlusion sites on MRA influence the efficacy of intravenous low-dose (0.6 mg/kg) alteplase therapy for ischemic stroke. *Int J Stroke*. 2009;4:In press.
4. Kent DM, Selker HP, Ruthazer R, Bluhmki E, Hacke W. The stroke-thrombolytic predictive instrument: a predictive instrument for intravenous thrombolysis in acute ischemic stroke. *Stroke*. 2006;37: 2957–2962.
5. Sylaja PN, Dong W, Grotta JC, Miller MK, Tomita K, Hamilton S, Semba C, Hill MD. Safety outcomes of Alteplase among acute ischemic stroke patients with special characteristics. *Neurocrit Care*. 2007;6: 181–185.
6. Wahlgren N, Ahmed N, Eriksson N, Aichner F, Bluhmki E, Dávalos A, Erilä T, Ford GA, Grond M, Hacke W, Hennerici MG, Kaste M, Köhrmann M, Larrue V, Lees KR, Machnig T, Roine RO, Toni D, Vanhooren G; Safe Implementation of Thrombolysis in Stroke-MOnitoring STudy Investigators. Multivariable analysis of outcome predictors and adjustment of main outcome results to baseline data profile in randomized controlled trials: Safe Implementation of Thrombolysis in Stroke-MOnitoring STudy (SITS-MOST). *Stroke*. 2008;39:3316–3322.
7. Ahmed N, Wahlgren N, Brainin M, Castillo J, Ford GA, Kaste M, Lees KR, Toni D; SITS Investigators. Relationship of blood pressure, antihypertensive therapy, and outcome in ischemic stroke treated with intravenous thrombolysis. Retrospective analysis from Safe Implementation of Thrombolysis in Stroke–International Stroke Thrombolysis Register (SITS-ISTR). *Stroke*. 2009;40:2442–2449.
8. Kimura K, Iguchi Y, Shibazaki K, Terasawa Y, Inoue T, Uemura J, Aoki J. Large ischemic lesions on diffusion-weighted imaging done before intravenous tissue plasminogen activator thrombolysis predicts a poor outcome in patients with acute stroke. *Stroke*. 2008;39:2388–2391.
9. Guideline Committee for Intravenous rt-PA (alteplase) in Acute Ischemic Stroke. Guidelines for intravenous application of rt-PA (alteplase) [in Japanese]. *Jpn J Stroke*. 2005;26:327–354.
10. The 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.
11. Barber PA, Demchuk AM, Zhang J, Buchan AM; for the ASPECTS Study Group. Validity and reliability of a semiquantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. *Lancet*. 2000;355:1670–1674.
12. Barber PA, Hill MD, Eliasziw M, Demchuk AM, Pexman JH, Hudon ME, Tomanek A, Frayne R, Buchan AM; ASPECTS Study Group. Imaging of the brain in acute ischaemic stroke: comparison of computed tomography and magnetic resonance diffusion-weighted imaging. *J Neurol Neurosurg Psychiatry*. 2005;76:1528–1533.
13. Wahlgren N, Ahmed N, Dávalos A, Ford GA, Grond M, Hacke W, Hennerici MG, Kaste M, Kuelkens S, Larrue V, Lees KR, Roine RO, Soinne L, Toni D, Vanhooren G; SITS-MOST investigators. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. *Lancet*. 2007;369:275–282.
14. Edaravone Acute Infarction Study Group. Effect of a novel free radical scavenger, edaravone (MCI-186), on acute brain infarction. Randomized, placebo-controlled, double-blind study at multicenters. *Cerebrovasc Dis*. 2003;15:222–229.
15. Albers GW, Bates VE, Clark WM, Bell R, Verro P, Hamilton SA. Intravenous tissue-type plasminogen activator for treatment of acute stroke: the Standard Treatment with Alteplase to Reverse Stroke (STARS) study. *JAMA*. 2000;283:1145–1150.
16. Hill MD, Buchan AM; Canadian Alteplase for Stroke Effectiveness Study (CASES) Investigators. Thrombolysis for acute ischemic stroke: results of the Canadian Alteplase for Stroke Effectiveness Study. *CMAJ*. 2005; 172:1307–1312.
17. Ribo M, Molina C, Montaner J, Rubiera M, Delgado-Mederos R, Arenillas JF, Quintana M, Alvarez-Sabín J. Acute hyperglycemia state is associated with lower tPA-induced recanalization rates in stroke patients. *Stroke*. 2005;36:1705–1709.
18. Poppe AY, Majumdar SR, Jeerakathil T, Ghali W, Buchan AM, Hill MD; Canadian Alteplase for Stroke Effectiveness Study Investigators. Admission hyperglycemia predicts a worse outcome in stroke patients treated with intravenous thrombolysis. *Diabetes Care*. 2009;32:617–622.
19. Yong M, Kaste M. Association of characteristics of blood pressure profiles and stroke outcomes in the ECASS-II trial. *Stroke*. 2008;39: 366–372.
20. Martin-Schild S, Hallevi H, Albright KC, Khaja AM, Barreto AD, Gonzales NR, Grotta JC, Savitz SI. Aggressive blood pressure-lowering treatment before intravenous tissue plasminogen activator therapy in acute ischemic stroke. *Arch Neurol*. 2008;65:1174–1178.
21. Rubiera M, Ribo M, Delgado-Mederos R, Santamarina E, Delgado P, Montaner J, Alvarez-Sabín J, Molina CA. Tandem internal carotid artery/middle cerebral artery occlusion: an independent predictor of poor outcome after systemic thrombolysis. *Stroke*. 2006;37:2301–2305.
22. Saqqur M, Uchino K, Demchuk AM, Molina CA, Garami Z, Calleja S, Akhtar N, Orouk FO, Salam A, Shuaib A, Alexandrov AV; CLOTBUST Investigators. Site of arterial occlusion identified by transcranial Doppler predicts the response to intravenous thrombolysis for stroke. *Stroke*. 2007;38:948–954.

わが国における脳卒中再発予防のための急性期内科治療戦略の確立に関する研究
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**「多施設共同研究 1：rt-PA 患者登録研究」**
**本研究成果の学会発表一覧、演題抄録**

4th Korean-Japanese Joint Stroke Conference, Fukuoka, 2008/11/21-23

1. Koga M, Toyoda K, Naganuma M, et al: Nationwide survey for hyperacute blood pressure lowering in patients with intracerebral hemorrhage in Japan.

18th European Stroke Conference, Stockholm, Sweden, 2009/5/26-29

2. Koga M, Toyoda K, Naganuma M, et al: Expert opinions on hyperacute blood pressure lowering in patients with intracerebral hemorrhage.
3. Toyoda K, Naganuma M, Koga M, et al: Stroke features and outcome of 600 patients receiving intravenous low-dose rt-PA for ischemic stroke: a Japanese multicenter observational study.

International Stroke Conference 2010, San Antonio, USA, 2009/2/24-26

4. Koga M, Kimura K, Shibasaki K, et al: Lower CHADS2 score is associated with favorable clinical outcome after intravenous rt-PA therapy in stroke patients with AF.
5. Koga M, Naganuma M, Shiokawa Y, et al: Low-dose intravenous rt-PA therapy for stroke patients out of the indications by the European licence: the SAMURAI study.
6. Naganuma M, Koga M, Shiokawa Y, et al: Reduced estimated glomerular filtration rate is associated with stroke outcomes after intravenous low-dose rt-PA: the Stroke Acute Management with Urgent Risk-factor Assessment and Improvement (SAMURAI) Study.
7. Nezu T, Koga M, Kimura K, et al: Pre-treatment DWI-ASPECTS has a relation with functional outcome at 3 months following intravenous rt-PA therapy.
8. Nezu T, Koga M, Kimura K, et al: Pre-treatment DWI-ASPECTS is superior to ct-aspects in detecting excellent to fairly good outcome after intravenous rt-PA therapy.
9. Mori M, Naganuma M, Okada Y, et al: Predictors of acute clinical deterioration in stroke patients receiving intravenous low-dose rt-PA: a multicenter observational study.
10. Yamagami H, Koga M, Shiokawa Y, et al: Impact of antiplatelet pre-treatment on intracranial hemorrhage and stroke outcome after intravenous thrombolysis: the Stroke Acute Management with Urgent Risk-factor Assessment and Improvement (SAMURAI) Study.

第 3 回 tPA 研究会、松江、2009/3/22

11. 祢津智久、古賀政利、永沼雅基、他：　DWI-ASPECTS における領域別早期虚血変化と rt-PA 静注療法後の脳梗塞患者の転帰。

第 50 回日本神経学会総会、仙台　2009/5/20-22

12. 古賀政利、豊田一則、永沼雅基、他：　わが国における急性期脳出血患者に対する降圧療法の現状。
13. 豊田一則：　rt-PA 静注療法の効果と限界。　（シンポジウム）

第 8 回日本頸部脳血管治療学会、北九州、2009/5/29-30
14. 祢津智久、古賀政利、木村和美、他： DWI-ASPECTS で評価した早期虚血変化と rt-PA 静注療法後の脳梗塞患者の転帰：わが国における脳卒中再発予防のための急性期内科治療戦略の確立に関する研究（SAMURAI 研究）。
15. 山上 宏、古賀政利、苅尾七臣、他： t-PA 静注療法施行例における発症前抗血栓療法と頭蓋内出血の関係：SAMURAI 後ろ向き研究の結果から。

第 28 回 Mt Fuji Workshop on CVD 東京 2009/8/22
16. 古賀政利、豊田一則 塩川芳昭、他： 急性期脳出血患者の降圧療法に関する全国アンケート調査。
17. 豊田一則： 脳内出血急性期の至適血圧。 （セミナー）
18. 西山和利、塩川芳昭、豊田一則、他： 本邦における rt-PA 静注療法後の脳出血・出血性梗塞に関する多施設共同研究。

第 12 回日本栓子検出と治療学会. 大阪, 2009/10/9-10
19. 加藤 貴之、秋山久尚、長谷川泰弘, 他： rtPA 静注療法の効果に寄与する因子の検討：SAMURAI Study。
20. 古賀政利、永沼雅基、塩川芳昭、他： 脳梗塞患者への低用量 rt-PA 静注療法に関する国内多施設共同後ろ向き観察研究：SAMURAI 研究、全体成績。
21. 芝崎謙作, 木村和美, 豊田一則, 他： 心房細動を有する急性期脳梗塞患者における rt-PA 静注療法。
22. 中川原 譲二, 豊田一則、古賀政利, 他： t-PA 静注療法の転帰に関する多施設共同検討：脳梗塞病型、梗塞サイズ・部位、閉塞病変の影響。
23. 永沼雅基、古賀政利、塩川芳昭、他： 腎機能障害は脳梗塞 rt-PA 静注療法後 36 時間以内の頭蓋内出血および 3 ヶ月後の転帰不良と関係する：SAMURAI Study。
24. 祢津智久、古賀政利、木村和美、他： rt-PA 静注療法例での早期虚血変化の評価：CT-ASPECTS と DWI-ASPECTS に差はあるか？ Stroke Acute Management with Urgent Riskfactor Assessment and Improvement(SAMURAI) Study.
25. 野田 智子、奥田聡, 塩川芳昭, 他： t-PA 静注療法施行例におけるエダラボンの使用状況について：SAMURAI Study。
26. 古井英介、矢澤由加子、板橋 亮、他： アルテプラーゼ静注療法開始 24 時間以内の抗血栓薬。
27. 森真由美、永沼雅基、岡田靖、他： 脳梗塞 rt-PA 静注療法 24 時間後の早期増悪に関わる因子の検討：SAMURAI Study.

第 21 回日本脳循環代謝学会総会, 大阪 2009/11/19-20
28. 牧原典子、岡田 靖、古賀政利、他： rt-PA 静注療法施行症例におけるスタチン使用の実態と頭蓋内出血・転帰に与える影響に関する研究—Stroke Acute Management with Urgent Risk-factor Assessment and Improvement (SAMURAI) Study－。

第 37 回日本救急医学会、盛岡、2009/10/29-31
29. 加藤貴之、秋山久尚、長谷川泰弘、他： 脳梗塞に対する rtPA 静注療法の転帰に Weekend effect はあるか？

第 35 回日本脳卒中学会総会、盛岡、2010/4/15-17

30. 上山 憲司、中川原 譲二、古賀 政利、他： t-PA静注療法の転帰-脳梗塞病型、梗塞サイズ・部位、閉塞病変の影響-：SAMURAI rt-PA Registry。
31. 遠藤 薫、古賀 政利、坂井 信幸、他： 主幹脳動脈閉塞による急性期脳梗塞患者の実態に関する多施設共同調査：SAMURAI・JR-NET2 合同調査。
32. 加藤 貴之、秋山 久尚、長谷川 泰弘、他： rtPA静注療法におけるWeekend effectの有無についての検討。
33. 古賀 政利、木村 和美、芝崎 謙作、他： 心房細動合併脳梗塞患者において$CHADS_2$スコアはrt-PA静注療法後の転帰と関連する。
34. 豊田 一則： 脳出血の急性期内科治療：降圧と凝血学的治療 （シンポジウム）。
35. 永沼 雅基、古賀 政利、峰松 一夫、他： 腎機能障害は脳梗塞rt-PA静注療法後の転帰不良に関連する：SAMURAI rt-PA Registry。
36. 滑川 道人、苅尾 七臣、古賀 政利、他： 脳梗塞においては rt-PA 治療前の収縮期血圧が長期予後を規定する：SAMURAI rt-PA Registry。
37. 野田智子、奥田 聡、古賀 政利、他：t-PA静注療法施行例におけるエダラボンの効果：SAMURAI rt-PA Registry。
38. 牧原典子、岡田 靖、古賀政利、他： スタチンの発症前服用および脂質値が rt-PA 静注療法後の転帰に及ぼす影響：SAMURAI rt-PA Registry。
39. 宮城 哲哉、古賀 政利、塩川 芳昭、他： 脳底動脈閉塞症例に対する低用量rt-PA静注療法の成績：SAMURAI研究。
40. 森 真由美、永沼 雅基、岡田 靖、他： rt-PA静注療法 24 時間後の脳梗塞早期増悪とその関連因子：SAMURAI rt-PA Registry。
41. 山上 宏、古賀 政利、豊田 一則： t-PA静注療法施行例における発症前抗血小板薬療法と頭蓋内出血の関係：SAMURAI rt-PA Registry。
42. 山上 宏、坂井 信幸、遠藤 薫、他： 主幹脳動脈閉塞による急性期脳梗塞例に対する治療法と予後との関係：SAMURAI・JR-NET2 合同調査。

第 4 回 tPA 研究会、盛岡、2010/4/17

43. 豊田 一則、古賀政利、塩川芳昭、他： 国内多施設共同登録研究 Stroke Acute Management with Urgent Risk-factor Assessment and Improvement (SAMURAI) rt-PA Registry：全体成績とサブ研究の紹介。

第 9 回日本頸部脳血管治療学会、横浜、2010/4/23-24

44. 遠藤 薫、古賀 政利、坂井 信幸、他： 内頸動脈閉塞による急性期脳梗塞患者の実態に関する多施設共同調査。

第 51 回日本神経学会総会、東京、2010/5/20-22

45. 古賀政利、永沼雅基、塩川芳昭、他： 欧州指針で rt-PA 静注療法適応外の脳梗塞患者における低用量 rt-PA 静注療法の成績：SAMURAI 研究。
46. 永沼雅基、森真由美、祢津智久、他： 透析患者の脳梗塞に対する rt-PA 静注療法：SAMURAI 研究。
47. 祢津智久、古賀政利、岡田靖、他： rt-PA 静注療法治療前の CT と DWI を用いた ASPECTS の比較：SAMURAI 研究。
48. 前田 亘一郎、古賀 政利、苅尾 七臣、他： 心房細動を有する脳出血患者における抗凝固療法の再開に関する全国調査。

≪抄録集≫

4th Korean-Japanese Joint Stroke Conference, Fukuoka, 2008/11/21-23

1. **Koga M, Toyoda K, Naganuma M, et al: Nationwide survey for hyperacute blood pressure lowering in patients with intracerebral hemorrhage in Japan.**

Purpose: Although acute hypertension is a major determinant of hematoma enlargement and poor clinical outcome in patients with intracerebral hemorrhage (ICH), there is no established strategy for the control of blood pressure (BP) during the acute phase. We conducted a nation-wide survey to reveal the expert opinions on the hyperacute antihypertensive treatment (AHT) in ICH patients.
Methods: The questionnaires in terms of the AHT strategies were sent to the responsible neurosurgeons/neurologists for stroke management in 1424 hospitals authorized by the Japan Neurosurgical Society, Societas Neurologica Japonica, and Japan Stroke Society. We report the interim results.
Results: Of 403 responders, 376 (93%) belonged to the hospital where acute ICH patients were managed. Of them, 374 responders (99.5%) agreed with AHT within 24 hours, and 315 (84%) started AHT immediately after the initial imaging. The threshold of systolic BP (SBP) for the initiation of AHT and the goal of SBP lowering were 160 and 150 mmHg in median, respectively. The most commonly used IV drug was nicardipine (59%), followed by diltiazem (33%); though a label of nicardipine in Japan does not recommend its usage for hyperacute ICH. As a second choice, 26% more responders chose nicardipine. Most responders who chose nicardipine (95%) reported that the drug has advantage in the power of BP reduction.
Conclusions: The expert opinions in Japan indicated that practical strategies for hyperacute BP reduction in ICH patients, including the target BP and the choice for antihypertensive agents, were different from the recommendations by the AHA and Japanese guidelines.

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18th European Stroke Conference, Stockholm, Sweden, 2009/5/26-29

2. **Koga M, Toyoda K, Naganuma M, et al: Expert opinions on hyperacute blood pressure lowering in patients with intracerebral hemorrhage.**

Background: Acute hypertension is a major determinant of hematoma enlargement and poor clinical outcome in patients with intracerebral hemorrhage (ICH). It remains unknown, however, how to control blood pressure (BP) during the acute phase of ICH. We conducted a nationwide web questionnaire survey to reveal expert opinions on this issue in Japan. Methods: We sent the questionnaires to neurosurgeons, neurologists and others responsible for ICH management in 1424 hospitals authorized by the Japan Stroke Society, Japan Neurosurgical Society, and Societas Neurologica Japonica in July, 2008.
Results: Of 600 responders, 92% belonged to hospital where they managed acute ICH patients. Of them, 99.6% agreed with starting antihypertensive treatment within 24 hours after ICH onset, and 85% started it at an emergency room or CT/MRI room immediately after the diagnosis of ICH was made. Most of them answered that the threshold of SBP for the initiation of antihypertensive treatment was at 180 mmHg (36%) or 160 mmHg (31%), being significantly different between neurosurgeons (median 160 mmHg, n=456) and neurologists/others (180 mmHg, n=92; $p<0.001$). The goal of SBP lowering was also biphasic, $\leq$ 160 mmHg (29%) and $\leq$ 140 mmHg (30%), being also different between neurosurgeons (median $\leq$ 150 mmHg) and neurologists/others ($\leq$ 160 mmHg, $p<0.001$). Nicardipine was the first choice intravenous drug for 57% and the second choice for 27% of the responders. Twenty six percent answered, however, that nicardipine use is inappropriate mainly because of the Japanese official label

contraindicating the use of nicardipine for hyperacute ICH patients while active intracranial bleeding continues. Conclusions: Japanese expert opinions especially by neurosurgeons recommended more aggressive BP lowering than indicated by the EUSI and AHA/ASA recommendations for acute ICH patients. Nicardipine was the most frequently used antihypertensive agent, but this was in conflict with the Japanese official label.

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18th European Stroke Conference, Stockholm, Sweden, 2009/5/26-29

3. **Toyoda K, Naganuma M, Koga M, et al: Stroke features and outcome of 600 patients receiving intravenous low-dose rt-PA for ischemic stroke: a Japanese multicenter observational study.**

Background: For patients with acute ischemic stroke, IV rt-PA therapy using 0.6 mg/kg alteplase was approved in Japan in 2005. We conducted an observational study to clarify the actual conditions of this low-dose rt-PA therapy in major stroke centers.
Methods: Consecutive stroke patients treated with rt-PA from October 2005 (time of the approval) through July 2008 were registered from 10 Japanese stroke centers located without regional imbalance.
Results: A total of 600 stroke patients (377 men, 72±12 years in age) were studied, which occupied ≈4.4% of overall rt-PA-treated patients in Japan. Median baseline ASPECTS (perfect score of 10) was 10 on baseline CT (IQR 8 – 10, for 503 patients) and 9 on DWI (7 – 10, for 498 patients). The internal carotid artery was occluded in 16.5%, M1 in 28.4%, and M2 in 19.4% for 546 patients evaluated mainly using MRA. IV antihypertensive drugs were used just before rt-PA for 27.6% of patients, and IV edaravone, a free radical scavenger, was used in the hyperacute stage for 83.7%. Mean NIHSS scores decreased from 13 (IQR 7 – 19) before rt-PA to 8 (3 – 16) 24 h later. Any intracranial hemorrhage (ICH) developed in 19.8% of patients (PH1 5.0%, PH2 3.5%); symptomatic ICH with ≥1-point increase in NIHSS within 36 h developed in 3.7%. The leading stroke subtype at the final diagnosis was cardioembolism (63.3%). At 3 months, 37 patients (6.2%) were dead. For 469 patients (39.2%) with a premorbid mRS score ≤ 1 and without dropout for follow-up, 184 (39.2%) had a mRS score ≤ 1 at 3 months; when patients with ≥81 years or those with the baseline NIHSS score ≥25 were excluded from the analysis according to the criteria by SITS-MOST, 43.1% had the score ≤ 1.
Conclusions: In our multicenter survey, 3-month outcome of patients receiving low-dose IV rt-PA therapy using 0.6 mg/kg alteplase was similar to or better than those from Western trials and post-approval surveys using a dose of 0.9 mg/kg and that from a Japanese nationwide post-approval survey (unpublished interim report).

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International Stroke Conference 2010, San Antonio, USA, 2009/2/24-26

4. **Koga M, Kimura K, Shibasaki K, et al: Lower CHADS2 score is associated with favorable clinical outcome after intravenous rt-PA therapy in stroke patients with AF.**

Background: $CHADS_2$ score is useful to predict the risk of ischemic stroke in patients with atrial fibrillation (AF). This study aimed to test whether $CHADS_2$ score can predict clinical outcome following intravenous alteplase (rt-PA) therapy in patients with AF.
Methods: A retrospective, multicenter, observational study was conducted to clarify the actual conditions of IV rt-PA therapy in 10 major stroke centers in Japan. Studied were a total of 218 consecutive stroke patients with AF (126 men, 74±10 years old) who were independent in

activities of daily living corresponding to a modified Rankin Scale (mRS) ≤2 before symptom onset , and treated with intravenous rt-PA from October 2005 through July 2008. $CHADS_2$ score was calculated from five risk factors as follows: 2 points for prior ischemic stroke and 1 point for each of patients aged ≥75 years, with hypertension, with diabetes mellitus and with congestive heart failure. The outcomes were: any intracerebral hemorrhage (ICH) defined as CT evidence of new ICH within the initial 36 hours; symptomatic ICH with an increase of ≥1 point from the baseline NIHSS score; chronic independency at 3 month corresponding to mRS ≤2; and cardiovascular events, including stroke recurrence, within 3 months after rt-PA therapy.
Results: The median $CHADS_2$ score was 2 (IQR 1-2). The distribution of patients with each $CHADS_2$ score was: score of 0, 16.0%; 1, 30.3%; 2, 29.4%; 3, 13.3%; 4, 8.7%; 5, 2.3%; and 6, 0%. The median (IQR) of initial NIHSS score was 14.5 (9-20) in total, and it was 12 (7-17) in patients with $CHADS_2$ score of 0, 15 (9-20) with the score of 1, 14.5 (9.25-20.75) with the score of 2 and 16 (10.5-20.5) with the scores of 3 to 5 (p=0.30). Any ICH (symptomatic ICH) was found in 20.0% (2.9%), 27.3% (4.6%), 39.1% (10.9%) and 26.4% (0%) of patients by each $CHADS_2$ category as above, respectively. Chronic independency assessed from 193 patients who had available information was found in 62.5%, 44.1%, 32.1% and 32.6%, respectively (p=0.023). Cardiovascular events occurred in 0%, 0%, 11.9% and 9.4%, respectively. After multivariate adjustment by sex and initial NIHSS score, $CHADS_2$ score was inversely associated with chronic independency at 3 months (per 1 point increase in numerical order; OR 0.76, 95% CI 0.58-0.98; p=0.040).
Conclusion: Lower $CHADS_2$ score was associated with chronic independency at 3 months after intravenous rt-PA therapy in stroke patients with AF.

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International Stroke Conference 2010, San Antonio, USA, 2009/2/24-26

5. **Koga M, Naganuma M, Shiokawa Y, et al: Low-dose intravenous rt-PA therapy for stroke patients out of the indications by the European licence: the SAMURAI study.**

Background: European regulatory agencies do not advocate intravenous recombinant tissue plasminogen activator (rt-PA) therapy in patients with severe stroke with NIH stroke scale (NIHSS) score ≥25, age >80 years, and having prior stroke with concomitant diabetes, unlike the US and Japanese labelings. This study aimed to document clinical outcomes in patients treated with low-dose intravenous rt-PA (alteplase, 0.6 mg/kg) within 3 hours of stroke onset who met exclusion criteria of the above European licence.
Methods: A retrospective, multicenter, observational study was conducted to clarify the efficiency of intravenous low-dose rt-PA therapy in clinical practice in 10 major stroke centers in Japan. Studied were a total of 600 consecutive stroke patients (377 men, 72±12 years old) who were treated with rt-PA from October 2005 through July 2008. Of all the patients, 422 patients (292 men, 68±10 years old) satisfied inclusion criteria of the European licence (In-group) and 178 patients (85 men, 82±9 years old) did not (Ex-group). Baseline characteristics and clinical outcomes were compared between the two groups. Symptomatic intracerebral hemorrhage (ICH) was defined as CT evidence of new ICH within the initial 36 hours with an increase of '1 point from the baseline NIHSS score. Chronic favorable outcome was assessed by modified Rankin Scale (mRS) 0-2 at 3 months after rt-PA therapy; this outcome was evaluated only for patients who were independent (mRS 0-2) prior to stroke onset.
Results: Of 178 patients in Ex-group, 40 had severe stroke with NIHSS ≥25, 129 were >80 years old, and 25 had prior stroke and concomitant diabetes. Hypertension (68% vs. 59%, p=0.032), diabetes (24% vs. 16%, p=0.032), and atrial fibrillation (53% vs. 40%, p=0.004) were

more common and hyperlipidemia (17% vs. 23%, p=0.108) was less common in Ex-group than In-group. Percentage ofpatients with premorbid mRS 0-2 was 83% in Ex-group and 98% in In-group (p=0.0001), and initial median NIHSS score was 16 and 11 (p<0.0001), respectively. As clinical outcomes, any ICH (symptomatic ICH) was observed in 15% (2%) of Ex-group and in 22% (5%) of In-group [p=0.037 (p=0.189)]. Chronic favorable outcome was found in 36% of Ex-group and 55% of In-group (p=0.0001) and mortality at 3 month was 13% and 5% (p<0.001), respectively.
Conclusion: Three-month functional and vital outcomes after low-dose rt-PA therapy in patients out of the indications by the European licence were less favorable compared with those in the others, although ICH was less common in the former than in the latter.

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International Stroke Conference 2010, San Antonio, USA, 2009/2/24-26

6. **Naganuma M, Koga M, Shiokawa Y, et al: Reduced estimated glomerular filtration rate is associated with stroke outcomes after intravenous low-dose rt-PA: the Stroke Acute Management with Urgent Risk-factor Assessment and Improvement (SAMURAI) Study.**

Background: The goal of this study was to determine whether renal dysfunction affects the outcome of stroke patients treated with intravenous (IV) low-dose recombinant tissue plasminogen activator (rt-PA).
Methods: A retrospective, multicenter, observational study (the Stroke Acute Management with Urgent Risk-factor Assessment and Improvement [SAMURAI] Study) was conducted to identify effects of underlying risk factors on rt-PA therapy using 0.6 mg/kg alteplase in 10 major stroke centers in Japan. A total of 554 consecutive stroke patients (358 men, 71±12 years) with a premorbid modified Rankin Scale (mRS) ≤2 who received IV rt-PA from October 2005 through July 2008 were studied. Renal dysfunction was defined as reduced estimated glomerular filtration rate (eGFR) <60 ml/min/1.73m$^2$.
Results: Renal dysfunction was present in 173 patients (31.2 %). Patients with renal dysfunction were older (p<0.001), and more commonly had hypertension (p<0.001), atrial fibrillation (p=0.002), prior ischemic heart disease (p=0.004) and prior use of antithrombotic agents (p<0.001) than patients without renal dysfunction. In renal dysfunction patients, any intracranial hemorrhage (ICH, 28.3% vs 17.1%, p=0.003) and symptomatic ICH (8.1% vs 2.4%, p=0.004) within the initial 36 hours, as well as mortality at 3 month (12.7% vs 3.9%, p<0.001) were more common, and chronic independency at 3 month corresponding to mRS ≤2 was less common (44.5% vs 54.1%, p=0.044) than patents without renal dysfunction. After multivariate adjustment, renal dysfunction was independently related to any ICH (OR 1.82, 95%CI 1.16-2.86, p=0.009), symptomatic ICH (OR 2.93, 95% CI 1.10-8.13, p=0.033), and chronic mortality (OR 2.93, 95%CI 1.33 - 6.62, p=0.008), though it was not related to chronic independency (OR 0.78, 95%CI 0.51 – 1.20, p=0.255).
Conclusions: Reduced eGFR was an independent predictor of ICH within 36 hours and mortality at 3 months in ischemic stroke patients receiving low-dose IV rt-PA therapy.

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International Stroke Conference 2010, San Antonio, USA, 2009/2/24-26

7. **Nezu T, Koga M, Kimura K, et al: Pre-treatment DWI-ASPECTS has a relation with functional outcome at 3 months following intravenous rt-PA therapy.**

Background: ASPECTS is a score to evaluate the extent of early ischemic change (EIC) on CT as well as on diffusion-weighted MRI (DWI). The extent of EIC may have relation with functional outcome and symptomatic hemorrhagic transformation in patients with ischemic stroke after intravenous recombinant tissue plasminogen activator (rt-PA) therapy. DWI can more clearly delineate the extent of EIC within 3 hours after stroke onset as compared with CT. The aim of the present study was to evaluate whether a pre-treatment DWI-ASPECTS can predict functional outcome at 3 months following rt-PA therapy.
Methods: A retrospective, multicenter, observational study was conducted to clarify the practical conditions of IV rt-PA therapy using 0.6 mg/kg alteplase in 10 major stroke centers in Japan. Studied were a total of 498 consecutive stroke patients (328 men, 72±11 years) who were treated with intravenous rt-PA from October 2005 through July 2008, underwent MRI with DWI sequence before rt-PA therapy. Excluded were patients with fairly severe to severe disability, corresponding to a modified Rankin Scale (mRS) 4 and 5 before symptom onset. An ASPECTS (10 for no EIC and 0 for the largest EIC) was assessed on the initial DWI study. Primary outcome was mRS 0-3 at 3 months after stroke onset.
Results: Of 498 patients, 305 (61.2%) had excellent to fairly good outcome (mRS 0-3) at 3 months. They were younger ($p<0.001$), more frequently male ($p=0.012$), less hypertensive ($p=0.021$), and less commonly have atrial fibrillation ($p<0.001$) and internal carotid artery occlusion ($p<0.001$) than the other patients (mRS 4-6). Pre-treatment NIHSS score was lower ($p<0.001$) and DWI-ASPECTS was higher ($p<0.001$) in the patients with mRS 0-3 than in the others (mRS 4-6). The optimal cutoff score of DWI-ASPECTS to predict primary outcome was $\geq 7$ with a sensitivity of 88% and specificity of 39%, and the area under the receiver-operating characteristic curve was 0.644. After multivariate logistic regression analysis with sex, age, pre-treatment NIHSS score, hypertension, atrial fibrillation and internal cerebral artery occlusion, the pre-treatment DWI-ASPECTS $\geq 7$ was an independent predictor of mRS 0-3 at 3 months after rt-PA therapy (OR 2.88, 95% CI 1.68-5.00).
Conclusion: DWI-ASPECTS is useful to predict patients' chronic functional outcome following intravenous rt-PA therapy in this multicenter study.

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International Stroke Conference 2010, San Antonio, USA, 2009/2/24-26

8. **Nezu T, Koga M, Kimura K, et al: Pre-treatment DWI-ASPECTS is superior to ct-aspects in detecting excellent to fairly good outcome after intravenous rt-PA therapy.**

Background: ASPECTS is a quantitative topographic score to evaluate the extent of early ischemic change (EIC) in the middle cerebral arterial territory on CT as well as on diffusion-weighted MRI (DWI). DWI can more clearly delineate the extent of EIC within 3 hours after stroke onset as compared with CT. There were a few data regarding the comparison of ASPECTS between DWI and CT before rt-PA therapy in same patients so far. This study aimed at elucidating the relationship between DWI-ASPECTS and CT-ASPECTS before rt-PA therapy and their associations with chronic functional outcome.
Methods: A retrospective, multicenter, observational study was conducted to clarify the practical conditions of IV rt-PA therapy using 0.6 mg/kg alteplase in 10 major stroke centers in Japan.

Studied were a total of 381 consecutive patients with anterior circulation ischemic stroke (249 men, 72±11 years) who were treated with intravenous rt-PA from October 2005 through July 2008, underwent both MRI with DWI sequence and CT before rt-PA therapy. Excluded were patients with fairly severe to severe disability, corresponding to a modified Rankin Scale (mRS) 4 and 5 before symptom onset. The MRI study was performed immediately after the CT study. An ASPECTS (10 for no EIC and 0 for the largest EIC) was assessed on the initial DWI and CT studies. Chronic functional outcome was assessed with mRS at 3 months after stroke onset.
Results: Of 381 patients, 230 (60.4%) had excellent to fairly good outcome (mRS 0-3) at 3 months. The pre-treatment DWI-ASPECTS (median 8, IQR 6-9) was lower than the pre-treatment CT-ASPECTS (9, 8-10) ($P<0.001$). DWI-ASPECTS was positively related with CT-ASPECTS ($r= 0.565$, $p<0.001$). The optimal cutoff score of DWI-ASPECTS to predict the patients with mRS 0-3 at 3 months was ≥7 with a sensitivity of 86% and specificity of 45%, and the area under the receiver-operating characteristic (ROC) curve was 0.681. On the other hand, the optimal cutoff score of CT-ASPECTS was ≥9 with a sensitivity of 76% and specificity of 48%, and the area under the ROC curve was 0.636.
Conclusion: DWI-ASPECTS had a positive relationship with CT-ASPECTS, but the former scored lower points than the latter. DWI-ASPECTS may be useful to predict excellent to fairly good outcome (mRS 0-3) at 3 months with higher sensitivity as compared with CT-ASPECTS.

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International Stroke Conference 2010, San Antonio, USA, 2009/2/24-26

9. **Mori M, Naganuma M, Okada Y, et al: Predictors of acute clinical deterioration in stroke patients receiving intravenous low-dose rt-PA: a multicenter observational study.**

Background and Purpose: The goal of this study was to determine clinical factors which contribute to acute neurological deterioration of stroke patients receiving intravenous (IV) low-dose recombinant tissue plasminogen activator (rt-PA) therapy.
Methods: A retrospective, multicenter, observational study was conducted to clarify the efficiency of IV rt-PA therapy using 0.6 mg/kg alteplase in clinical practice in 10 major stroke centers in Japan (Stroke Acute Management with Urgent Risk-factor Assessment and Improvement [SAMURAI] Study group). A total of 566 consecutive stroke patients (355 men, 72±12 years old) treated with IV rt-PA from October 2005 through July 2008 whose 24-hour National Institute of Health Stroke Scale (NIHSS) score was available were studied. Acute deterioration was defined as 4 point or more increase in NIHSS score at 24 hour from the baseline NIHSS score.
Results: Acute deterioration was present in 56 patients (9.9 %, 38 men, 72±12 years old). Median baseline NIHSS score was 11 (IQR 7-16) in the patients with acute deterioration, and 13 (IQR 7-19) in those without ($p=0.047$). The patients with acute deterioration more commonly had diabetes mellitus ($p=0.010$), hyperlipidemia ($p=0.035$), internal carotid artery (ICA) occlusion ($p<0.001$), and prior use of oral hypoglycemic agents ($p=0.028$) and statin ($p=0.022$) than the patients without deterioration. After multivariate analysis, acute deterioration was independently related to baseline NIHSS score (OR 0.92, 95%CI 0.87-0.97 per 1-point increase, $p=0.003$), systolic blood pressure (1.19, 1.01-1.41 per 10-mmHg increase, $p=0.040$), diabetes mellitus (2.44, 1.18-4.92, $p=0.014$), ICA occlusion (6.96, 3.34-14.81, $p<0.001$). In the patients with acute deterioration, any intracranial hemorrhage (ICH, 42.9% vs. 17.5%, $p<0.001$) and symptomatic ICH (19.6% vs. 2.2%, $p<0.001$) within the initial 36 hours, as well as mortality at 3 months (25.0% vs. 4.3%, $p<0.001$) were more common, and independent activity of daily living, corresponding to modified Rankin Scale (mRS) ≤2, at 3 months was less common (8.7%

vs. 58.5%, p<0.001) than those without deterioration.
Conclusions: Lower baseline NIHSS score, higher systolic blood pressure, diabetes mellitus, ICA occlusion were independent predictors of acute clinical deterioration in ischemic stroke patients receiving low-dose IV rt-PA therapy.

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International Stroke Conference 2010, San Antonio, USA, 2009/2/24-26

**10. Yamagami H, Koga M, Shiokawa Y, et al: Impact of antiplatelet pre-treatment on intracranial hemorrhage and stroke outcome after intravenous thrombolysis: the Stroke Acute Management with Urgent Risk-factor Assessment and Improvement (SAMURAI) Study.**

Background and Purpose: We sought to clarify the impact of antiplatelet (AP) pre-treatment on intracranial hemorrhage (ICH) and 3-month outcome after intravenous recombinant tissue plasminogen activator (rt-PA) therapy in patients with ischemic stroke.
Methods: In a retrospective, multicenter, observational study, we studied data from consecutive patients treated with low-dose intravenous rt-PA (0.6 mg/kg alteplase) which was approved in Japan, within 3h after symptom onset. AP therapy previous to thrombolysis was obtained from clinical records. Any ICH was defined as CT evidence of new ICH within the initial 36 hours, and symptomatic ICH (sICH) with neurological deterioration corresponding to an increase of ≥1 point from the baseline NIHSS score. Favorable outcome reflecting independence was defined as a modified Rankin Scale score of 2 or less at 3 months.
Results: Of the 600 patients (377 men, 72 ± 12 years old) treated with rt-PA, 189 (31.5%) used AP drugs prior to thrombolysis; 159 (26.5%) used aspirin and 14 were pre-treated with dual AP drugs. Both ICH and sICH occurred more frequently in patients with AP pre-treatment than those not (ICH: 26.5% vs 16.8%, P = 0.008, sICH: 8.5% vs 1.7%, P < 0.001). Particularly, 8 of 14 patients (57.1%) who had received dual AP drugs developed ICH. In multivariate analysis, AP pre-treatment was an independent predictor of ICH (OR 1.69, 95% CI 1.05 – 2.71) and sICH (OR 6.06, 95% CI 2.22 – 16.5). Favorable outcome was fewer in patients with AP pre-treatment than those not (40.7% vs 50.4%, P=0.03), whereas it was not an independent predictor after multivariate analysis.
Conclusion: In Japanese patients, AP therapy previous to thrombolysis was associated with occurrence of ICH and sICH, and may lead to poor outcome, even though using low-dose rt-PA.

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第 3 回 tPA 研究会、松江、2009/3/22

**11. 祢津智久、古賀政利、永沼雅基、他：　DWI-ASPECTS における領域別早期虚血変化と rt-PA 静注療法後の脳梗塞患者の転帰。**

【目的】急性期脳梗塞患者の早期虚血変化は、血栓溶解療法の適応判定に有用であり、CT や MRI で広範な早期虚血変化が生じた症例は転帰不良とされている。MRI 拡散強調画像(DWI)における ASPECTS 領域ごとの虚血変化の有無と脳卒中重症度、転帰の関係を検討した。
【方法】対象は我々の研究班に属する 10 施設で 05 年 10 月から 08 年 7 月までに rt-PA 治療を受けた 600 例中、発症前 modified Rankin scale(mRS)0-1 で rt-PA 治療前に MRI を施行した 400 例(71±11 歳、男性 269 例)。ASIST-JAPAN が提唱する ASPECTS DWI 11 部位で虚血変化を評価し、3 か月後の mRS 0-1 を転帰良好、2-6 を転帰不良とした。
【成績】治療直前 NIHSS 値は中央値 13(IQR 7－19)、転帰良好は 156 例(39%)であった。

ASPECTS DWI は中央値 9(IQR 7－10)で、ROC 曲線で求めた転帰不良を示す閾値は 6 であった。ASPECTS DWI 7 以上の症例の 56%、6 以下の症例の 83%が転帰不良であった(年齢、性、治療直前 NIHSS 補正後 OR 2.1、95%CI 1.1-4.3)。ASPECTS DWI 各虚血変化のうち内包以外の 10 部位では、所見陽性例は陰性例に比べ治療直前 NIHSS が高値であった(全て p<0.05)。転帰不良を予測するのに、年齢、性のみの補正では、レンズ核(転帰良好 16%対 不良 25%、OR 1.9、95%CI 1.1-3.3)、島(31%対 43%、OR 1.7、95%CI 1.1-2.6)、M1(8%対 24%、OR 3.3、95%CI 1.8-6.5)、M2(15%対 25%、OR 2.0、95%CI 1.2-3.5)、M3(9%対 15%、OR 2.1、95%CI 1.1-4.2)、M4(7%対 17%、OR 2.3、95%CI 1.2-5.0)、M5(19%対 32%、OR 1.8、95%CI 1.1-2.9)の虚血陽性例が多かったが、年齢、性、治療直前 NIHSS で補正すると M1 の虚血所見のみが有意に転帰不良を予測し得た(OR 2.3、95%CI 1.2-4.8)。
【結論】rt-PA 静注療法後の転帰不良を予測する ASPECTS DWI の値は 6 以下であった。M1 の早期虚血変化は年齢、性、治療直前 NIHSS で補正した後も転帰不良例に有意に多く、転帰を予測する上で重要な所見と考えられた。

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第 50 回日本神経学会総会、仙台　2009/5/20-22

**12. 古賀政利、豊田一則、永沼雅基、他：　わが国における急性期脳出血患者に対する降圧療法の現状**

目的：急性期脳出血患者に対する降圧療法の現状を調べる。
方法：全国 1424 病院を対象に急性期脳出血の血圧管理に関するアンケート調査を行った。
結果：42%の有効回答があり、うち 92%が急性期脳出血診療に従事していた。99.6%が発症 24 時間以内の降圧を肯定した。降圧を開始する収縮期血圧（SBP）として 180mmHg 以上(36%)と 160mmHg 以上(31%)が多く、目標 SBP では 160mmHg 以下(29%)と 140mmHg 以下(30%)が多かった。57%が第 1 選択降圧剤に経静脈投与ニカルジピンを選択した一方で、26%は禁忌項目のためにニカルジピンを使用しにくいと回答した。
結論：わが国ではガイドラインよりも積極的な降圧が一般的であった。また、添付文書で使用が制限されているニカルジピンが頻用されていた。

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第 50 回日本神経学会総会、仙台　2009/5/20-22

**13. 豊田一則：　rt-PA 静注療法の効果と限界。　（シンポジウム）**

急性期虚血性脳卒中に対する組織型プラスミノゲン・アクティベータ（tissue-type plasminogen activator, tPA：アルテプラーゼ）の静注療法は、2005 年 10 月の国内承認より既に 3 年を過ぎ、わが国でも標準治療として定着しつつある。この治療の普及を契機に国内の脳卒中診療体制の不備が明らかになり、病院前救護を含めた医療環境を改善する起爆剤となった点でも意義が大きい。国内外の同治療の成績をおおまかにまとめると、「tPA 静注療法後の症候性頭蓋内出血は 1 割未満で、3 ヵ月後に約 4 割の患者が完全自立している一方、1～2 割が死の転帰をとる」と言える。このうち発症 3 カ月後の完全自立（mRS 0-1）の割合は、EU の市販後調査である SITS-MOST と国内市販後調査（中間解析）でともに 39%を占め（SITS-MOST の症例選択基準に基づく）、0.9 mg/kg の投与量の欧米と 0.6 mg/kg の国内で同じ治療効果を得られたことは興味深い。わが国では治療適応の検討に MRI が用いられることが多いが、拡散強調画像での早期虚血所見や MRA での頭頸部血管閉塞部位と治療効果の関係も症例の蓄積とともに次第に明らかになってきた。厚生労働科学研究「わが国における脳卒中再発予防のための急性期内科治療戦略の確立に関する研究」で参加 10 施設の 600 例を解析した共同研究の成績をまじ

えて、tPA 静注療法の功罪と今後の展望を解説する。

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第 8 回日本頸部脳血管治療学会、北九州、2009/5/29-30

**14. 祢津智久、古賀政利、木村和美、他：　DWI-ASPECTS で評価した早期虚血変化と rt-PA 静注療法後の脳梗塞患者の転帰：わが国における脳卒中再発予防のための急性期内科治療戦略の確立に関する研究（SAMURAI 研究）**

【目的】急性期脳梗塞患者の早期虚血変化は血栓溶解療法の適応判定に有用であり、CT や MRI で広範な早期虚血変化が生じた症例は転帰不良とされている。MRI 拡散強調画像(DWI)における ASPECTS での虚血変化と rt-PA 静注療法後の転帰の関係を検討した。
【方法】対象は我々の研究班に属する 10 施設で 05 年 10 月から 08 年 7 月までに rt-PA 治療を受けた脳梗塞患者 600 例中、発症前 modified Rankin scale (mRS) 0-2 で rt-PA 治療前に MRI を施行した 420 例(71±11 歳、男性 280 例、うち心原性脳塞栓症 257 例[61%])。DWI-ASPECTS 10 点法で虚血変化を評価し、3 か月後の mRS 0-2 を転帰良好とした。
【成績】治療直前 NIHSS 値は中央値 12(IQR 7－19)、DWI-ASPECTS は中央値 8(IQR 7－10)であった。転帰良好は 221 例(53%)で、他の 199 例と比較して年齢、心房細動、治療直前 NIHSS、DWI-ASPECTS、内頚動脈閉塞で有意差を認めた（各々P<0.001, 単変量解析)。ROC 曲線で求めた転帰良好を予測する DWI-ASPECTS の閾値は 7 点（感度 88%, 特異度 33%, AUC 0.627）であり、DWI-ASPECTS 7 以上の 60%、6 以下の 22%が転帰良好であった。DWI-ASPECTS 7 以上は転帰良好と関連し（年齢、性補正後 OR 3.64, 95%CI 2.19-6.22)、治療直前 NIHSS、心房細動、内頚動脈閉塞で補正後も有意に転帰良好に関連した（OR 1.93, 95%CI 1.06-3.54)。心原性脳塞栓症に限った検討でも、DWI-ASPECTS 7 以上（感度 85%,特異度 41%, AUC 0.649）は転帰良好に独立して関連した（OR 2.32, 95%CI 1.14-4.82)。
【結論】国内多施設共同研究において、rt-PA 静注療法前の DWI-ASPECTS 7 以上が、脳梗塞患者の転帰良好に独立して関連した。心原性脳塞栓症に限った場合も、同様であった。

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第 8 回日本頸部脳血管治療学会、北九州、2009/5/29-30

**15. 山上　宏、古賀政利、苅尾七臣、他：　t-PA 静注療法施行例における発症前抗血栓療法と頭蓋内出血の関係：SAMURAI 後ろ向き研究の結果から**

目的：発症 3 時間以内の急性期脳梗塞に対して tPA 静注療法を施行された症例において、発症前の抗血栓薬投与が頭蓋内出血合併および予後に及ぼす効果を検証すること。
方法：「我が国における脳卒中再発予防のための急性期内科治療戦略の確立に関する研究（SAMURAI 研究）」の参加 10 施設において 2005 年 10 月から 2008 年 7 月までに t-PA 静注療法を施行された 600 例（平均年齢 71.8±11.8 歳、男性 377 例）を対象とし、脳梗塞発症前の抗血小板薬および抗凝固薬の投与と、頭蓋内出血、症候性頭蓋内出血の発生および 3 ヶ月後の機能予後との関係について検討した。
結果：脳梗塞発症前に抗血栓薬が投与されていたのは 225 例（37.5%）で、抗血小板薬が 189 例（31.5%)、抗凝固薬が 53 例（8.8%）であった。抗血小板薬の種類ではアスピリンが 159 例（26.5%）と最も多く、抗血小板薬単剤投与は 158 例（26.3%)、抗血小板薬 2 剤併用は 14 例（2.3%）であった。36 時間以内の全ての頭蓋内出血は抗血小板薬投与例で非投与例に比して有意に多く（26.5% vs 16.8%, P=0.008)、特に 2 剤併用していた 14 例中 8 例（57.1%）で頭蓋内出血を合併していた。多変量解析で頭蓋内出血の独立した危険因子は、心房細動(OR 2.21)、発症前抗血小板薬投与（OR 1.69）および tPA 投与

終了時の収縮期血圧（OR 1.02, P=0.009）であった。また、症候性頭蓋内出血の合併も抗血小板薬投与例で有意に多く（8.5% vs 1.7%, P<0.001）、多変量解析では唯一の独立した危険因子であった(OR 6.06)。抗血 小板薬投与例では、3ヶ月後の機能予後良好例(mRS 0-2)が有意に少なかったが(41.6% vs 52.6%, P=0.02)、独立した危険因子ではなかった。
結論：急性期脳梗塞に対する tPA 静注療法において、発症前の抗血小板薬投与は頭蓋内出血および症候性頭蓋内出血の危険因子である。

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第 28 回 Mt Fuji Workshop on CVD　東京　2009/8/22

**16. 古賀政利、豊田一則　塩川芳昭、他：　急性期脳出血患者の降圧療法に関する全国アンケート調査**

【目的】急性期脳出血では血圧高値が転帰不良に関連しているが、確立した血圧コントロール指針はない。急性期脳出血患者に対する降圧療法の現状を調べる。
【方法】全国 1424 病院（全ての日本脳神経外科学会専門医訓練 A 項・C 項施設、日本脳卒中学会認定研修教育病院、日本神経学会教育施設・准教育施設・教育関連施設）を対象に急性期脳出血の血圧管理に関する WEB アンケート調査を 2008 年 7 月に行った。
【結果】有効回答率は 42%であった。回答者の 79%が脳神経外科医で、92%が急性期脳出血診療に従事していた。急性期従事者の 99.6%が発症 24 時間以内の降圧療法を肯定した。85%は緊急外来や CT/MRI 室で脳出血の診断確定後速やかに降圧を開始していた。降圧開始の目安とする収縮期血圧（SBP）として 180mmHg 以上(36%)と 160mmHg 以上(31%)の回答が多く、60%の回答者がガイドラインの推奨値である 180mmHg 以上よりも低い値で降圧を開始していた。脳神経外科医以外（神経内科医など）の降圧目安は中央値 180mmHg 以上であったが、脳神経外科医は 160mmHg 以上とより積極的に降圧を開始していた（p<0.001）。降圧目標の SBP として 160mmHg 以下(29%)と 140mmHg 以下(30%)の回答が多く、38%の回答者が 140mmHg、130mmHg もしくは 120mmHg 以下の積極的な降圧を選択した。57%がニカルジピンを第 1 選択経静脈投与降圧剤とし、第 2 選択まであわせて 84%がニカルジピンを使用していた一方で、26%が「禁忌項目のためにニカルジピンは使用しにくい」と回答した。
【結論】わが国の診療現場では、ガイドラインよりも急性期脳出血の降圧に積極的であった。添付文書で使用が制限されているニカルジピンが第一選択薬であった。

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第 28 回 Mt Fuji Workshop on CVD　東京　2009/8/22

**17. 豊田一則：　脳内出血急性期の至適血圧　（セミナー）**

脳出血急性期の血圧上昇は血腫や血腫周囲の浮腫を拡大させ、また脳卒中再発や他の心血管病を惹起することによって、予後を増悪させ得る。一方で、急性期降圧によって血腫周囲に低潅流、虚血を招くことも懸念されるが、総じて急性期血圧高値は予後不良と考えられる。国内や米国のガイドラインでは、明らかなエビデンスを欠くものの 180/105 mmHg を急性期降圧開始の目安としているが、降圧目標値は定まっていない。血圧管理の明確なエビデンスを得るべく、国外では現在 ATACH や INTERACT などの介入試験が組まれ、そのパイロット試験成績が公表されている。国内からは Ohwaki ら（Stroke 2004:35;1364）が、急性期脳出血患者 76 例の入院後 48 時間以内の血腫拡大に 48 時間以内の収縮期血圧最高値が独立して有意に関与しており、降圧の目安を 150 mmHg 以下に設定した患者の方が血腫拡大を起こし難かったと報告している。われわれは急性期に静注降圧治療を行った脳出血患者を、最初の 24 時間以内の収縮期血圧平均値を用いて四等分して 3 週間後の予後を比べ、多要因での補正後も収縮期血圧平均値がもっとも低か

った群（<138 mmHg）はもっとも高かった群（≥158 mmHg）に比べて 3 週間後に完全自立に復する割合が有意に高かった（Itabashi R, et al. J Hypertens, 2008;26:2016-2021）。またわれわれの研究班で行った全国アンケート調査では、降圧開始の目安とする収縮期血圧として 180mmHg 以上(36%)と 160mmHg 以上(31%)の回答が多く、降圧目標値として 160mmHg 以下(29%)と 140mmHg 以下(30%)の回答が多く、57%がニカルジピンを第 1 選択経静脈投与降圧剤とし、第 2 選択まであわせて 84%がニカルジピンを使用していた（Koga M, et al: Hypertens Res 2009 Epub ahead of print）。このアンケートに示された降圧目標値や降圧薬の妥当性と安全性を調べる多施設共同の前向き観察研究を、今夏開始した。

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第 28 回 Mt Fuji Workshop on CVD　東京　2009/8/22

**18. 西山和利、塩川芳昭、豊田一則、他：　本邦における rt-PA 静注療法後の脳出血・出血性梗塞に関する多施設共同研究。**

【目的】rt-PA 静注療法（tPA 療法）は脳梗塞超急性期治療として本邦においても根付いてきたが、出血性合併症が最大の問題点の一つであり、特に脳出血や出血性梗塞の合併は出血性合併症の中でも最も忌避すべき病態である。本邦の tPA 療法は欧米のプロトコールとは異なる用量を用いるので、本邦での tPA 療法後に生じた脳出血・出血性梗塞（脳出血）を検討することは臨床的に大きな意義がある。
【方法】「わが国における脳卒中再発予防のための急性期内科治療戦略の確立に関する研究」班に参加している脳卒中診療拠点病院 10 施設での資料を用いる。これら施設で、本邦における tPA 静注療法が認可されて以来、2008 年 7 月までに実施されたすべての tPA 療法症例を脳出血の観点から後方視的に調査する。
【結果】総計 10 施設、600 症例が調査対象となった。脳出血の合併は 19.3%であった。脳出血合併の関連因子を検討したところ、性別、年齢、体重は関連しないが、原病が心原性脳梗塞であることは脳出血合併の因子となった。元の脳梗塞巣が小さいほど脳出血は合併しにくい傾向があった。画像診断上の ASPECT-DWI は脳出血合併と相関したが、ASPECT-CT は相関しなかった。脳梗塞病変が中大脳動脈領域にあることは脳出血の合併と相関するが、責任血管と脳出血の間には大きな相関を認めなかった。治療直前の降圧療法の実施歴、心疾患を有することは脳出血の合併と相関した。さらに脳出血の合併はその重症度に関わらず、退院時の機能予後不良と相関した。
【結論】本邦での tPA 療法も欧米のプロトコールと同様に合併症として脳出血を生じやすいが、そうした出血に関して一定の解析結果を見出すことが出来た。

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第 12 回日本栓子検出と治療学会. 大阪, 2009/10/9-10

**19. 加藤　貴之、秋山久尚、長谷川泰弘, 他：　rtPA 静注療法の効果に寄与する因子の検討：SAMURAI　Study**

【目的】rtPA 静注療法では発症後の早期の静注開始が転帰の改善に寄与するとされる。施設共同研究の data から rtPA 静注療法の効果に寄与する因子を検討した。【方法】2005 年 10 月から 2008 年 7 月に rtPA 静注療法をうけた基幹病院 10 施設の 600 例を対象とした。①静注後の神経症状改善（NIHSS の 2 点以上の減少）、②3 ヶ月後の ADL（mRS 0 - 1）に関与する諸因子を、得られた data よりロジスティック回帰分析で検討した。【結果】①については年齢（OR：0.98　P＝0.023）、糖尿病（OR：0.597　P＝0.03）が関連した。②については年齢（OR：0.968　P=0.001）、高血圧（OR：0.602　P=0.024）、入院時 NIHSS（OR：0.891　P=0.000）、糖尿病（OR：0.542　P＝0.034）が有意に関連した。

しかし、いずれにおいても発症から静注開始までの時間と転帰との間に関連はみられなかった。病型別にみると非心原性脳塞栓症（N＝220 例）において発症から静注開始までの時間と静注後の神経症状改善の有無との間に有意な関連がみられた（OR : 0.989　P＝0.029）。一方、心原性脳塞栓症（N＝380 例）では静注後の神経症状改善において糖尿病が有意な関連を示した（OR : 0.489　P=0.024）。【結論】心原性脳塞栓症では、糖尿病の寄与が相対的に強いため、発症から静注開始までの時間との関連がみられなかったものと思われる。急性期からの血糖管理が神経症状改善に寄与するかいなかは今後の検討を要する。

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**20. 古賀政利、永沼雅基、塩川芳昭、他：　脳梗塞患者への低用量 rt-PA 静注療法に関する国内多施設共同後ろ向き観察研究：SAMURAI 研究、全体成績**

【目的】わが国でのみ承認された脳梗塞患者への低用量 rt-PA 静注療法（アルテプラーゼ 0.6 mg/kg）の、多施設での治療成績を、後ろ向きに調査する。
【方法】厚生労働科研（H20–循環器等(生習) - 一般–019）に参加する国内 10 施設で、2005 年 10 月～2008 年 7 月に rt-PA 静注療法を受けた 600 例（男性 377 例、72±12 歳、治療前 NIHSS 中央値 13）を、対象とした。
【結果】36 時間以内の症候性頭蓋内出血を 23 例（3.8%, 95% CI 2.6 – 5.7%）に認め、3 か月後に 43 例(7.2%, 5.4 – 9.5%)が死亡していた。3 か月後に 199 例(33.2%, 29.5 – 37.0%)が完全自立（mRS 0-1）し、この頻度は発症前に完全自立していた 535 例では 37.2%（33.2 – 41.4%）、さらに欧州での使用基準（≤80 歳、NIHSS≤25 など）を満たす 399 例では 40.6%(35.9 – 45.5%)と増えた。多変量解析にて、若齢、NIHSS 低値、内頸動脈閉塞がないこと、CT での ASPECTS 高値、治療直前の降圧を要しないことが完全自立に、心不全と高血糖が死亡に、独立して有意に関連した。
【結論】本研究での症候性頭蓋内出血や 3 か月後の転帰は、国外の市販後調査と比べて同等以上の成績を示した。

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**21. 芝崎謙作，木村和美，豊田一則，他：　心房細動を有する急性期脳梗塞患者における rt-PA 静注療法**

【目的】心房細動(AF)を有する急性期脳梗塞患者における rt-PA 静注療法後の転帰について検討する。【方法】厚労省科学研究(H20-循環器等(生習)-一般-019)わが国における脳卒中再発予防のための急性期内科治療戦略の確立に関する研究に参加し行った（後ろ向き多施設共同観察研究）。対象は 2005 年 10 月～2008 年 8 月に rt-PA 静注療法を受けた患者。AF の有無により AF 群と非 AF 群に分け、背景因子、神経徴候の改善度、退院時の転帰について比較検討した。　【結果】245 例(男性 161 例、平均 71 歳)が本研究に登録された。AF 群は 111 例(45%)であった。AF 群は非 AF 群と比較し、高齢(74 vs. 69 歳、p=0.001)、女性(42% vs. 28%、p=0.016)が多く、t-PA 開始前の NIHSS スコアが高値であった(14 vs. 12、p=0.004)。また、rt-PA 著効例(入院 7 日目の NIHSS スコアが 0-1 点、あるいは 10 点以上の改善と定義)が AF 群で少なかった(33% vs. 46%、p=0.05)。症候性頭蓋内出血の頻度に差はなかった(4.5% vs. 5.2%、p=0.795)。退院時の転帰は、AF 群が予後不良(mRS スコア 4-5 と死亡と定義)の頻度が多かった(49% vs. 31%、p=0.006)。【結論】AF を有する急性期脳梗塞患者における rt-PA 静注療法後の転帰は、AF を有さない患者と比べて著効例も少なく転帰不良である。

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**22. 中川原　譲二, 豊田一則、古賀政利, 他：　t-PA 静注療法の転帰に関する多施設共同検討：脳梗塞病型、梗塞サイズ・部位、閉塞病変の影響**

【目的】MRI/MRA による急性期脳梗塞病変の評価に基づいて、t-PA 静注療法の 3 ヵ月後の転帰（mRS）に対する脳梗塞病型と梗塞のサイズ・部位および閉塞病変などの影響を評価した。【方法】対象は 10 施設で 05 年 10 月から 08 年 7 月までに t-PA 静注療法を受けた 600 例を対象とし、脳梗塞病型（心原性脳梗塞:CE、アテローム血栓症:AT、ラクナ梗塞:LA)、脳梗塞のサイズ（小、中、大)、脳梗塞の出現部位（皮質梗塞、穿通枝梗塞)、責任閉塞血管病変（内頸動脈:ICA、中大脳動脈: M1,M2）ごとに転帰を評価した。【結果】①脳梗塞病型では、LA の転帰が良好であった。CE と AT とを比較すると、転帰良好（mRS0,1）の頻度は同等であったが、前者で死亡の頻度が高かった。②脳梗塞の大きさは、転帰に対して有意に影響する因子であった。小梗塞・中大梗塞とも CE と AT の転帰良好の頻度は同程度であった。③梗塞出現部位では、AT による皮質枝梗塞と CE による穿通枝梗塞の転帰は比較的良好で、皮質枝＋穿通枝梗塞の転帰は不良であった。④M1、M2 閉塞症の転帰は比較的良好で、ICA 閉塞症の転帰は不良であった。また、M1、M2 閉塞症では CE よりも AT の転帰が良好であったが、ICA 閉塞症ではこの傾向は見られなかった。【結論】急性期脳梗塞患者に対する t-PA 静注療法では、脳梗塞病型と梗塞のサイズ・部位および閉塞病変ごとに転帰が異なる。ICA 閉塞症は病型によらず転帰が不良であり、本療法には限界がある。

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**23. 永沼雅基、古賀政利、塩川芳昭、他：　腎機能障害は脳梗塞 rt-PA 静注療法後 36 時間以内の頭蓋内出血および 3 ヶ月後の転帰不良と関係する：SAMURAI Study**

【目的】腎機能障害が rt-PA 静注療法後の転帰に与える影響を検討した。

【方法】多施設共同後ろ向き研究(SAMIRAI study)に登録された脳梗塞rt-PA静注療法連続 600 例中、発症前modified Rankin Scale(mRS)≦2 であった 554 例(71±12 歳、男性 358 例)。腎機能障害を推定GFR 60 ml/min/1.73m$^2$未満と定義し、治療後 36 時間以内のすべての頭蓋内出血(intracerebral hemorrhage: ICH)、症候性 ICH、3 ヶ月後転帰良好（mRS ≦2)、3 ヶ月後死亡との関係を調べた。

【結果】腎機能障害を 173 例(31.2%)に認めた。腎機能障害例はより高齢(p<0.001)で、高血圧(p<0.001)、心房細動(p=0.002)、虚血性心疾患の既往(p=0.004)、治療前抗血栓薬の使用(p<0.001)の割合が高値であった。腎機能障害例では、すべての ICH(28.3% vs 17.1%, p=0.003)、症候性 ICH(8.1% vs 2.4%, p=0.004)、3 ヶ月後死亡(12.7% vs 3.9%, p<0.001)が有意に高率で、3 ヶ月後転帰良好 (44.5% vs 54.1%, p=0.044)が有意に少なかった。多変量解析で、腎機能障害はすべての ICH(OR 1.86, 95%CI 1.18-2.92, p=0.008)、症候性 ICH (OR 3.53, 95% CI 1.20-11.4, p=0.026)、死亡(OR 2.93, 95%CI 1.33-6.62, p=0.010)に独立して関係した。

【結論】腎機能障害は、脳梗塞 rt-PA 静注療法後 36 時間以内の頭蓋内出血および 3 ヶ月後死亡と関連した。

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**24. 祢津智久、古賀政利、木村和美、他： rt-PA 静注療法例での早期虚血変化の評価：CT-ASPECTS と DWI-ASPECTS に差はあるか？ Stroke Acute Management with Urgent Riskfactor Assessment and Improvement(SAMURAI) Study**

【目的】脳梗塞急性期の早期虚血変化の評価に、CT や MRI 拡散強調画像(DWI)の ASPECTS が有用である。同一症例での CT と DWI の ASPECTS を比較した報告は少ない。我々は発症 3 時間以内に rt-PA 静注療法を実施した脳梗塞例の治療前 CT と DWI を用い、この問題を検討した。【方法】対象は、研究班に属する 10 施設で 05 年 10 月から 08 年 7 月までに rt-PA 静注療法を受けた脳梗塞患者 600 例中、発症前 modified Rankin scale (mRS) ≤3 の内頸動脈系梗塞で、治療前に CT と MRI の両者を撮像した 363 例(72±11 歳, 男性 210 例)である。両者の ASPECTS を比較し、3 か月後 mRS 0-3 を予測するカットオフ値を ROC 曲線解析で検討した。【結果】223 例 (61.4%)が 3 ヶ月後 mRS 0-3 であった。CT-ASPECTS（中央値 9、IQR 8-10)は DWI-ASPECTS（8、6-9)より高値で(P<0.001)、両者は相関した(r=0.58, P<0.001)。3 ヶ月後 mRS0-3 予測のカットオフ値は CT-ASPECTS 9 点（感度 77%,特異度 47%)、DWI-ASPECTS 7 点（感度 87%,特異度 48%）で、ROC 曲線 AUC は CT-ASPECTS で 0.63、 DWI-ASPECTS で 0.70 であった。【結論】早期虚血変化の評価において、DWI-ASPECTS は CT-ASPECTS より 1～2 点低得点となり、3 ヶ月後 mRS 0-3 の予測では DWI-ASPECTS で感度が高かった。

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**25. 野田　智子、奥田聡, 塩川芳昭, 他： t-PA 静注療法施行例におけるエダラボンの使用状況について：SAMURAI Study**

【目的】t-PA 静注療法施行症例における脳保護薬エダラボンの使用状況と、治療後の転帰や脳出血に与える影響について検討する。【方法】多施設後ろ向き研究（SAMURAI Study）において登録された、t-PA 静注療法を施行された連続 600 例において、エダラボン使用群と非使用群の予後、脳出血合併率について検討した。
【結論】エダラボンは 502 例（84%）に使用されていた。エダラボン使用群は非使用群に比べ若年で（平均年齢 71.2 歳 vs 74.8 歳, p=0.005）あったが、両群で t-PA 静注開始時の NIHSS の分布に有意差はなかった（p=0.29)。使用群は非使用群に比して、退院時および 3 か月後の modified Rankin Scale で予後良好（mRS 0-1）の割合が大きかった（退院時 32% vs 25%, p=0.12、3 ヶ月後 40% vs 34%, p=0.23)。予後不良群については退院時、3 か月後ともに使用群で少ない傾向がみられた(退院時 18% vs 27%, p=0.06、3 ヶ月後 17% vs 26%, P=0.075)。また脳出血の合併は使用群で少ない傾向が見られた(19% vs 24%, p=0.3)。【結論】t-PA 施行例におけるエダラボンの使用率は 84%と高かった。エダラボンは予後良好群を増やし、予後不良群、脳出血合併例を減らす傾向があるが、両群に統計学的な有意差は見られなかった。

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**26. 古井英介、矢澤由加子、板橋　亮、他： アルテプラーゼ静注療法開始 24 時間以内の抗血栓薬**

目的：国内基幹施設におけるアルテプラーゼ静注療法（IV rt-PA）開始 24 時間以内の抗血栓療法の現状を明らかにする.
方法：厚生労働科学研究（SAMURAI 研究, 主任研究者　豊田一則）に参加した 10 施