

2017 SNUH International Stroke Symposium

Hemorrhagic Transformation in Ischemic Stroke



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① Is hemorrhagic transformation bad ?

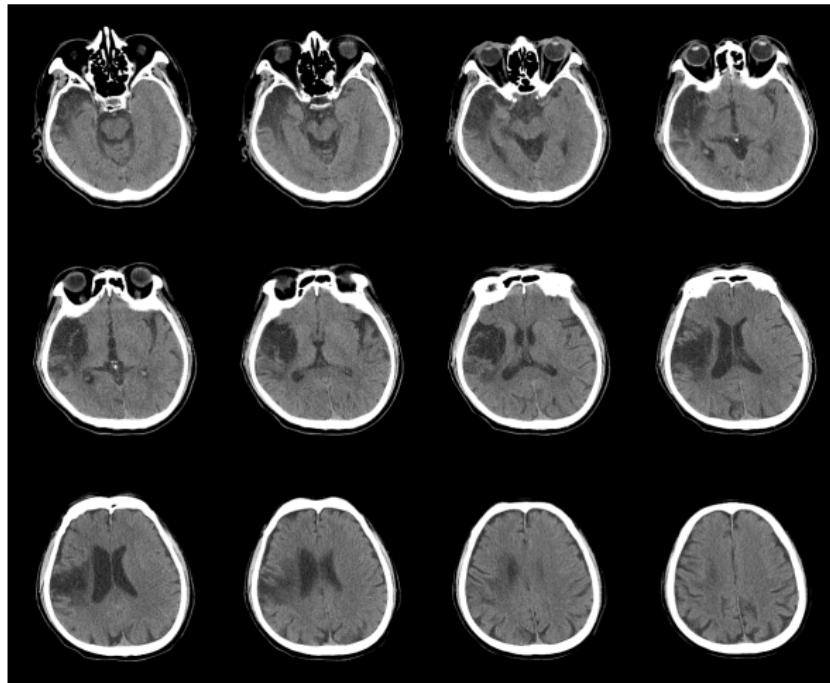
Table 3. Distribution of different types of HT related to early improvement/deterioration and tPA treatment

| | Non-tPA | tPA | Total |
|--|-------------|-----------------|----------------|
| <i>Deterioration >4 points on NIHSS</i> | | | |
| Non-HT | 7/81 (8.6%) | 0/16 (0%) | 7/97 (7.2%) |
| HT | 1/10 (10%) | 2/15 (13.3%) | 3/25 (12%) |
| Petechial | 0/4 | 1/8 | 1/12 |
| Confluent | 1/6 | 0/6 | 1/12 |
| Space-occupying | 0/0 | 1/1 | 1/1 |
| Total | 8/91 (8.8%) | 2/31 (6.5%) | 10/122 (8.2%) |
| <i>Improvement >4 points on NIHSS</i> | | | |
| Non-HT | 6/81 (7.4%) | 5/16 (31.3%) | 11/97 (11.3%) |
| HT | 1/10 (10%) | 7/15 (46.7%) | 8/25 (32%)* |
| Petechial | 0/4 | 4/8 | 4/12 |
| Confluent | 1/6 | 3/6 | 4/12 |
| Space-occupying | 0/0 | 0/1 | 0/1 |
| Total | 7/91 (7.7%) | 12/31 (38.7%)** | 19/122 (15.6%) |

* p = 0.011, ** p < 0.001.

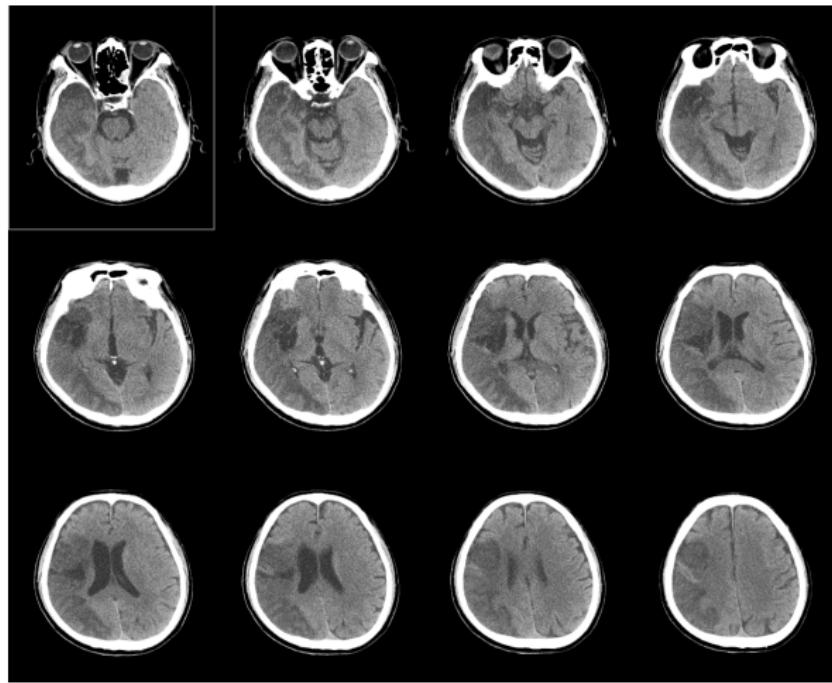
Among 122 consecutive stroke patients (mean age 65.5 years), 19 patients (15.6%) showed early improvement which was associated with the occurrence of Hemorrhagic Transformation (p = 0.011) and tPA treatment (p < 0.001)

68YO Male with Lt. distal ICA occlusion



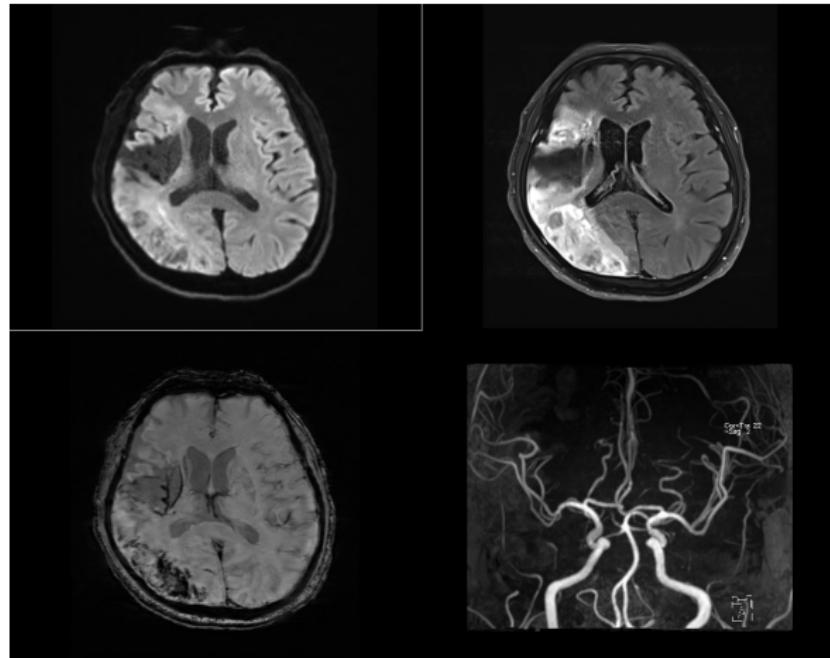
NIHSS 9: Facial palsy 1, LU 2, LL 2, Seosory 2, Dysarthria 1, Neglect 2

68YO Male with Lt. distal ICA occlusion, HD 7D



NIHSS 7: Facial palsy 1, LU 1, LL 1, Seosory 2, Dysarthria 1, Neglect 2

68YO Male with Lt. distal ICA occlusion, HD 18D



NIHSS 5: Facial palsy 1, LU 0, LL 0, Seosory 2, Dysarthria 1, Neglect 2

The Impact of Recanalization on Ischemic Stroke Outcome

A Meta-Analysis

Joung-Ho Rha, MD; Jeffrey L. Saver, MD

Comparison: 01 Recanalization vs. Non-Recanalization

Outcome: 04 Good Outcome by Time

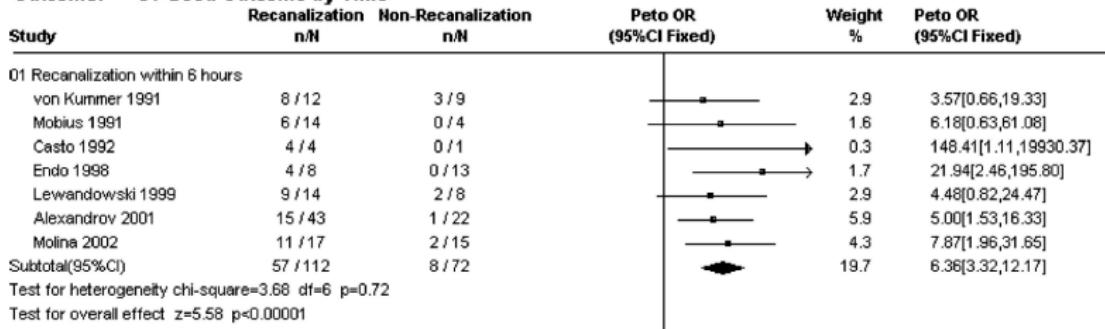


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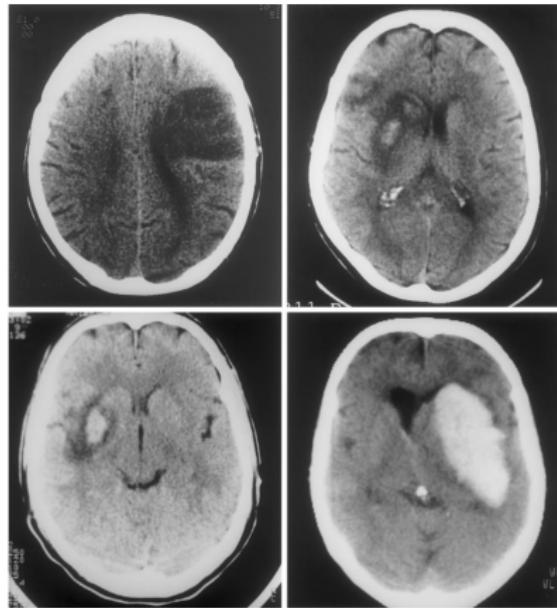
- 1 Definition
- 2 Prevalence
- 3 Prognosis
- 4 Predictors
- 5 Management
- 6 Summary

Imaging definition

- Hemorrhagic infarction type I:
Small hyperdense petechiae
- Hemorrhagic infarction type II:
More confluent hyperdensity throughout the infarct zone;
without mass effect
- Parenchymal hematoma type I:
Homogeneous hyperdensity occupying <30% of the infarct zone;
some mass effect
- Parenchymal hematoma type II:
Homogeneous hyperdensity occupying >30% of the infarct zone;
significant mass effect.

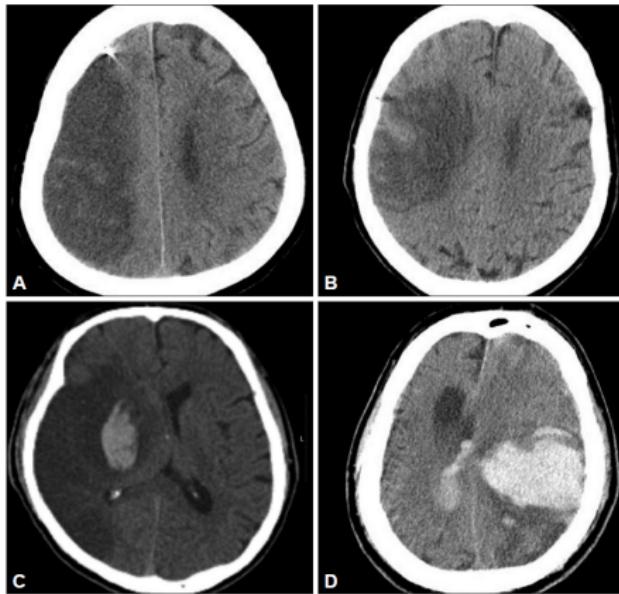
Fiorelli M. et al. Stroke. 1999;30:2280-2284

Imaging definition



Fiorelli M. et al. Stroke. 1999;30:2280-2284

Imaging definition



Lee JH, J Neurocrit Care 2013

Imaging definition

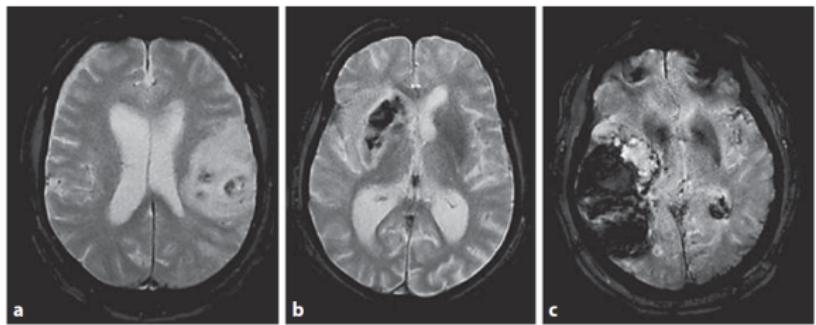


Fig. 1. The three categories of HT on T_2^* -MRI: petechial (a), confluent (b) and space-occupying (c).

Clinical definition

- Asymptomatic hemorrhagic transformation
- Symptomatic hemorrhagic transformation

NINDS study group *N Engl J Med* 1995; Hacke W. et al. *Lancet* 1998; Wahlgren N. et al. *Lancet* 2007

Clinical definition

- Asymptomatic hemorrhagic transformation
- Symptomatic hemorrhagic transformation
- Any clinical deterioration within 36 hours of symptom onset (NINDS)
- NIHSS score aggravation ≥ 4 within 7 days of onset (ECASS II)
- NIHSS score aggravation ≥ 4 within 36 hours or death within 24 hours (SITS-MOST)

NINDS study group *N Engl J Med* 1995; Hacke W. et al. *Lancet* 1998; Wahlgren N. et al. *Lancet* 2007

| | |
|-----------|---|
| ECASS 3 | Any hemorrhage with neurologic deterioration as indicated by an NIHSS score that was higher by ≥ 4 points than the value at baseline or the lowest value in the first 7 d or any hemorrhage leading to death; in addition, the hemorrhage must have been identified as the predominant cause of the neurologic deterioration |
| ECASS 2 | Blood at any site in the brain on the CT scan, documentation by the investigator of clinical deterioration, or adverse events indicating clinical worsening or causing a decrease in the NIHSS score of ≥ 4 points than the value at baseline or the lowest value in the first 7 d or any hemorrhage leading to death |
| SITS-MOST | Local or remote parenchymal hematoma Type 2 on the imaging scan obtained 22 to 36 hours after treatment plus neurologic deterioration as indicated by a score on the NIHSS that was higher by ≥ 4 points than the baseline value |
| NINDS | If a hemorrhage had not been seen on a previous CT scan but there was subsequently either a suspicion of hemorrhage or any decline in neurologic status |

Prevalence

| Clinical trial | Sample size | Duration of radiographic follow up | Asymptomatic hemorrhagic transformation rate | Symptomatic hemorrhagic transformation rate | Parenchymal hemorrhage type 2 rate | Time to treatment ^a |
|--------------------------------|-------------|------------------------------------|--|---|------------------------------------|--|
| IV FIBRINOLYSIS | | | | | | |
| NINDS | 312 | 7–10 days | 4.5% (14/312) | 6.4% (20/312) | N/A | 1.5 h ^b |
| ECASS-II | 409 | 7 days | 39.6% (161/407) | 8.8% (36/407) | 8.1% (33/407) | N/A |
| ATLANTIS | 272 | 18–30 h | 11.4% (31/272) | 70% (19/272) | N/A | 4.36 h ^b |
| SITS-MOST | 6483 | 22–36 h | 9.6% (617/6483) | 7.3% (468/6483) | 2.9% (184/6352) | 2.3 h ^b |
| ECASS-III | 418 | 36 h | 27% (113/418) | 2.4% (10/418) | 1.9% (8/418) | 3.98 h ^b |
| IST-III | 1515 | 7 days | N/A | 6.9% (104/1515) | N/A | 4.2 h ^b |
| IA FIBRINOLYSIS | | | | | | |
| PROACTI | 26 | 90 days | 50% (13/26) | 15.4% (4/26) | 7.7% (2/26) | 5.5 h ^b |
| PROACTII | 121 | 7–10 days | 68% (73/108) | 10% (11/108) | N/A | 4.5 h ^b |
| COMBINED IV/IA APPROACH | | | | | | |
| EMS | 17 | 7 ± 1 days | 11.8% (2/17) | 23.5% (4/17) | 0.0% (0/17) | 2.6 h ^b /6.3 h ^d |
| IMS-I | 80 | 36 h | 43% (34/80) | 6.3% (5/80) | 7.5% (6/80) | 1.33 h ^b /3.53 h ^d |
| IMS-II | 81 | 36 h | 32.1% (26/81) | 9.9% (8/81) | 8.6% (7/81) | 2.37 h ^b /N/A ^d |
| IMS-III | 434 | 24 ± 6 h | 27.4% (119/434) | 6.2% (27/434) | 5.8% (25/434) | 2.03 h ^b /N/A ^d |
| MECHANICAL THROMBECTOMY | | | | | | |
| Merci | | | | | | |
| Phase I | 28 | 24 h | 42.9% (12/28) | 0.0% (0/28) | 0.0% (0/28) | 6.25 h ^d |
| MERCI Trial | 141 | 24 h | 27.7% (39/141) | 78% (111/141) | 1.4% (2/141) | 6.4 h ^{*d} |
| Multi-MERCI | 164 | 24 h | 30.5% (50/164) | 9.8% (16/164) | 2.4% (4/164) | 5.9 h ^{*d} |
| Penumbra | | | | | | |
| Pivotal Stroke Trial | 125 | 24 h | 16.8% (21/125) | 11.2% (14/125) | 1.6% (2/125) | 4.85 h ^d |
| POST Trial | 157 | 24 h | 13.4% (21/157) | 6.4% (10/157) | N/A | 5.18 h ^d |
| Solitaire | | | | | | |
| Phase I | 20 | 24 h | 30% (6/20) | 10.0% (2/20) | 5.0% (1/20) | 6.7 h ^d |
| SWIFT Trial | 58 | 24 h | 15.5% (9/58) | 2.0% (1/58) | 0.0% (0/58) | 5.54 h ^{*d} |
| Trevo | | | | | | |
| TREVO | 60 | N/A | N/A | N/A | N/A | 5.03 h ^d |
| TREVO-2 | 88 | 18–36 h | 40.9% (36/88) | 4.5% (4/88) | 8.0% (7/88) | 5.4 h ^{*d} |

Sussman E.S. et al. Frontiers in Neurology 2013

Early Hemorrhagic Transformation of Brain Infarction: Rate, Predictive Factors, and Influence on Clinical Outcome Results of a Prospective Multicenter Study

Maurizio Paciaroni, MD; Giancarlo Agnelli, MD; Francesco Corea, MD, PhD; Walter Ageno, MD;
Andrea Alberti, MD; Alessia Lanari, MD; Valeria Caso, MD, PhD; Sara Micheli, MD;
Luca Bertolani, MD; Michele Venti, MD, PhD; Francesco Palmerini, MD; Sergio Biagini, MD;
Giancarlo Comi, MD; Paolo Previdi, MD; Giorgio Silvestrelli, MD, PhD

Background and Purpose—Early hemorrhagic transformation (HT) is a complication of ischemic stroke but its effect on patient outcome is unclear. The aims of this study were to assess: (1) the rate of early HT in patients admitted for ischemic stroke, (2) the correlation between early HT and functional outcome at 3 months, and (3) the risk factors for early HT.

Methods—Consecutive patients with ischemic stroke were included in this prospective study in 4 study centers. Early HT was assessed by CT examination performed at day 5 ± 2 after stroke onset. Study outcomes were 3-month mortality or disability. Disability was assessed using a modified Rankin score (≥ 3 indicating disabling stroke) by neurologists unaware of the occurrence of HT in the individual cases. Outcomes in patients with and without early HT were compared by χ^2 test. Multiple logistic regression analysis was used to identify predictors for HT.

Results—Among 1125 consecutive patients (median age 76.00 years), 98 (8.7%) had HT, 62 (5.5%) had hemorrhagic infarction, and 36 (3.2%) parenchymal hematoma. At 3 months, 455 patients (40.7%) were disabled or died. Death or disability was seen in 33 patients with parenchymal hematoma (91.7%), in 35 patients with hemorrhagic infarction (57.4%) as compared with 387 of the 1021 patients without HT (37.9%). At logistic regression analysis, parenchymal hematoma, but not hemorrhagic infarction, was independently associated with an increased risk for death or disability (OR 15.29; 95% CI 2.35 to 99.35). At logistic regression analysis, parenchymal hematoma was predicted by large lesions (OR 12.20, 95% CI 5.58 to 26.67), stroke attributable to cardioembolism (OR 5.25; 95% CI 2.27 to 12.14) or to other causes (OR 6.77; 95% CI 1.75 to 26.18), high levels of blood glucose (OR 1.01; 95% CI 1.00 to 1.01), and thrombolytic treatment (OR 3.54, 95% CI 1.04 to 11.95).

Conclusions—Early HT occurs in about 9% of patients. Parenchymal hematoma, seen in about 3% of patients, is associated with an adverse outcome. Parenchymal hematoma was predicted by large lesions attributable to cardioembolism or other causes, high blood glucose, and treatment with thrombolysis. (*Stroke*. 2008;39:2249-2256.)

Italian registry

- 1136 consecutive patients admitted within 12 hours of onset
- Median age: 76 YO
- CT at day 5 \pm 2 after onset
- Hemorrhagic transformation in 98 (8.7%)
- Hemorrhagic infarction in 62 (5.5%)
- Parenchymal hematoma in 36 (3.2%)

Paciaroni M. et al. Stroke 2008

Fiorelli et al Hemorrhagic Transformation Within 36 Hours of a Cerebral Infarct 2283

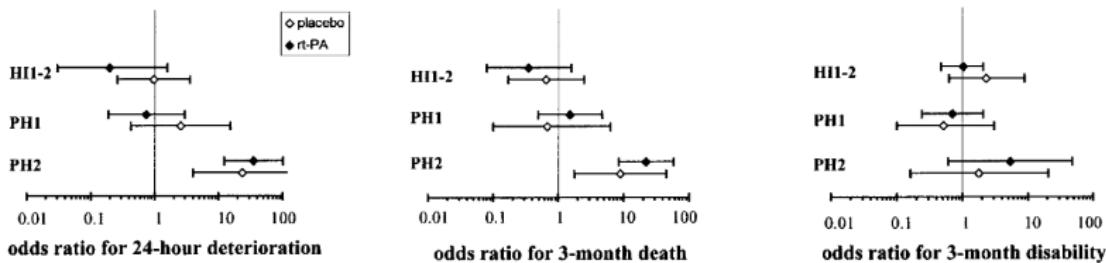
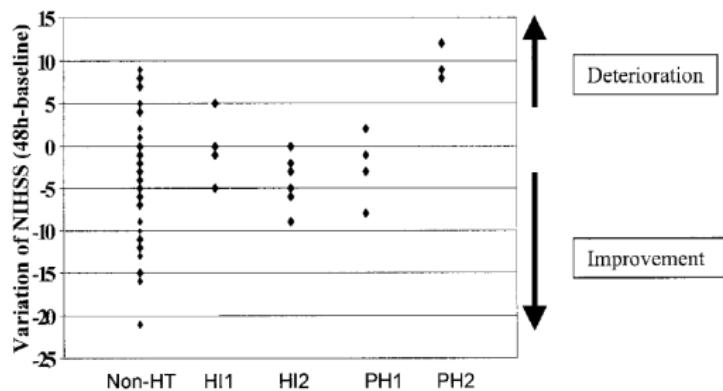
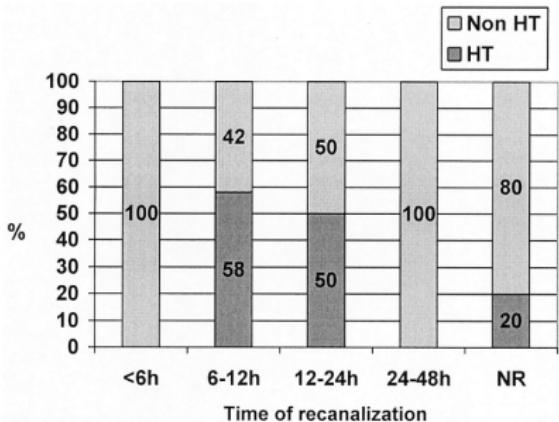


Figure 3. ORs and 95% CIs for 24-hour deterioration (decrease of the NIHSS score of ≥ 4 points compared with baseline), 3-month death, and 3-month disability (Rankin scale score of ≥ 2) in placebo and rtPA arms. ORs are adjusted for age and extent of early signs of infarct on baseline CT.

Compared with absence of hemorrhagic transformation, PH2 had a devastating impact on early neurological course (odds ratio for deterioration, 32.3; 95% CI, 13.4 to 77.7), and on 3-month death (odds ratio, 18.0; 95% CI, 8.05 to 40.1)

Timing of Spontaneous Recanalization and Risk of Hemorrhagic Transformation in Acute Cardioembolic Stroke

Carlos A. Molina, MD; Joan Montaner, MD; Sonia Abilleira, MD; Bernardo Ibarra, MD;
Francisco Romero, MD; Juan F. Arenillas, MD; José Alvarez-Sabín, MD



Italian registry

- At 3 months, 326 patients (29.2%) were disabled and 129 died (11.5%)
- Death or disability were seen
 - in 33 patients with parenchymal hematoma (91.7%),
 - in 35 of the patients with hemorrhagic infarction (57.4%)
 - as compared with 387 of the 1021 patients without hemorrhagic transformation (37.9%).

Paciaroni M. et al. Stroke 2008

Italian registry

Table 3. Results of Multivariate Analysis

| | OR | 95% CI |
|--|-------|---------------|
| Predictors of adverse outcome (dead or disability) | | |
| Age | 1.07 | 1.05 to 1.09 |
| History of diabetes | 2.10 | 1.38 to 3.19 |
| High NIHSS | 1.35 | 1.30 to 1.41 |
| Atherosclerosis | 1.84 | 1.15 to 2.93 |
| First-ever stroke | 0.50 | 0.31 to 0.79 |
| Parenchymal hematoma | 15.29 | 2.35 to 99.35 |

Paciaroni M. et al. Stroke 2008

① Is hemorrhagic transformation bad ?

- ① Is hemorrhagic transformation bad ?
- ② Is hemorrhagic transformation predictable ?

Italian registry

Predictors of HT

| | | |
|--------------------|------|--------------|
| Large lesion | 4.57 | 2.83 to 7.39 |
| Cardioembolism | 2.36 | 1.44 to 3.68 |
| Low platelet count | 1.01 | 1.01 to 1.08 |

Predictors of PH

| | | |
|------------------------------|-------|---------------|
| Large lesion | 12.20 | 5.58 to 26.67 |
| Cardioembolism | 5.25 | 2.27 to 12.14 |
| Other cause | 6.77 | 1.75 to 26.18 |
| High levels of blood glucose | 1.01 | 1.00 to 1.01 |
| Treatment with thrombolysis | 3.54 | 1.04 to 11.95 |

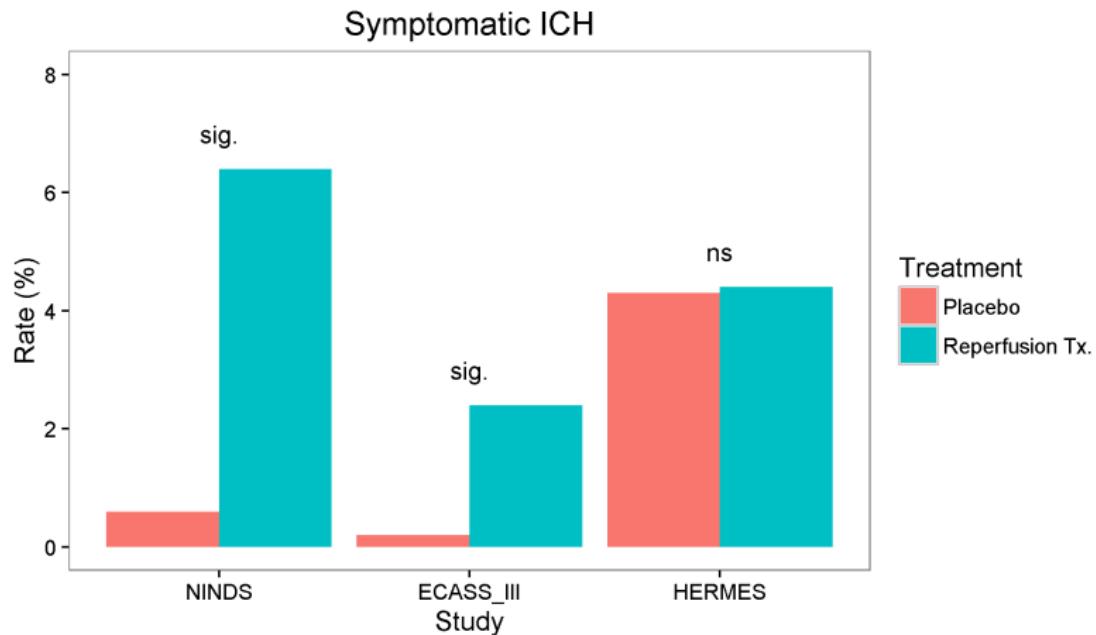
Paciaroni M. et al. Stroke 2008

Predictors for hemorrhagic transformation

- Old age
- Large infarction
- Severe neurologic deficit
- Cardioembolism
- High blood pressure
- Hyperglycemia
- Low LDL (in LAA)
- Poor collateral flow
- Low platelet count
- Medications: statin, anti-thrombotics

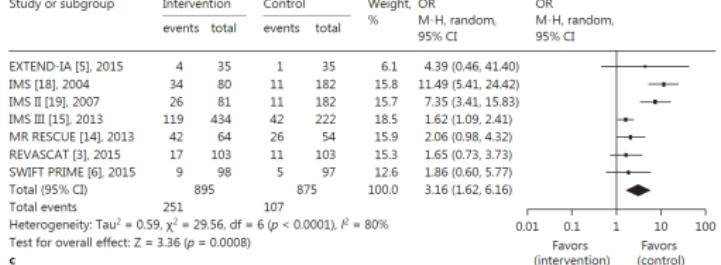
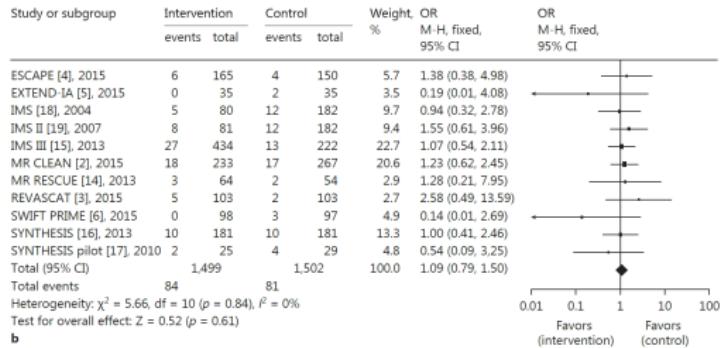
Mazya M. et al Stroke 2012; Larrue V. et al Stroke 2001; Paciaroni M. et al Stroke 2008; Kim BJ et al Stroke 2009; Jauch E.C. et al Stroke 2013; Zhang J et al Ann Transl Med 2014

Reperfusion therapy

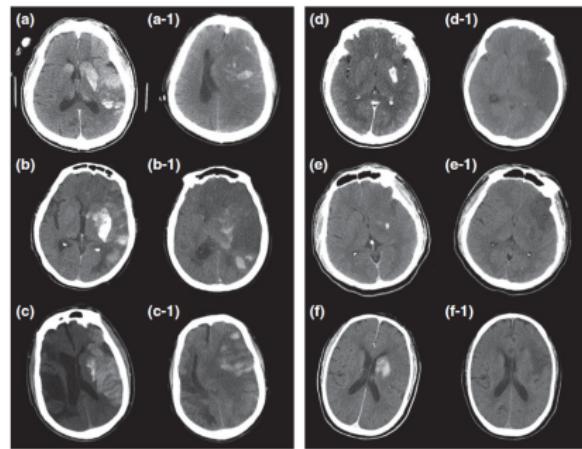


NINDS study group NEJM 1995; Hacke W et al. NEJM 2008; Goyal M et al. Lancet 2016

Symptomatic (b) and asymptomatic (c) hemorrhagic transformation



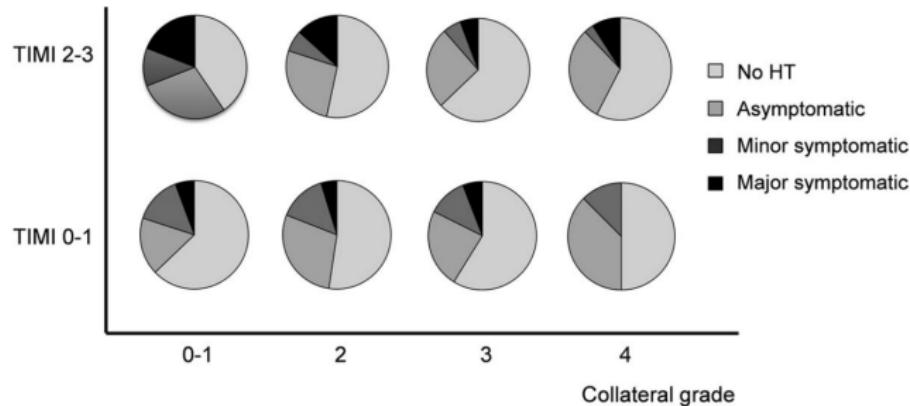
Cortical enhancement on CT



| | |
|---------------------------|-----|
| Sensitivity | 93% |
| Specificity | 52% |
| Positive predictive value | 39% |
| Negative predictive value | 96% |

Kim JM, et al European journal of Neurology 2016

Collateral flow averts hemorrhagic transformation



Hemorrhagic transformation was more frequently observed in patients with poor collaterals and recanalization than in other groups ($P = 0.048$).

Bang OY et al Stroke 2011

Risk Scores-GWTG

Risk Score for Intracranial Hemorrhage in Patients With Acute Ischemic Stroke Treated With Intravenous Tissue-Type Plasminogen Activator

Bijoy K. Menon, MD; Jeffrey L. Saver, MD; Shyam Prabhakaran, MD, MS; Mathew Reeves, PhD; Li Liang, PhD; DaiWai M. Olson, RN, PhD; Eric D. Peterson, MD; Adrian F. Hernandez, MD; Gregg C. Fonarow, MD; Lee H. Schwamm, MD; Eric E. Smith, MD, MPH

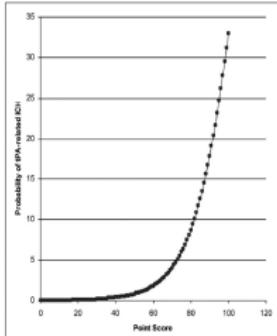
Background and Purpose—There are few validated models for prediction of risk of symptomatic intracranial hemorrhage (sICH) after intravenous tissue-type plasminogen activator treatment for ischemic stroke. We used data from Get With The Guidelines—Stroke (GWTG-Stroke) to derive and validate a prediction tool for determining sICH risk.

Methods—The population consisted of 10,242 patients from 988 hospitals who received intravenous tissue-type plasminogen activator within 3 hours of symptom onset from January 2009 to June 2010. This sample was randomly divided into derivation (70%) and validation (30%) cohorts. Multivariable logistic regression identified predictors of intravenous tissue-type plasminogen activator-related sICH in the derivation sample; model β coefficients were used to assign point scores for prediction.

Results—sICH within 36 hours was noted in 496 patients (4.8%). Multivariable adjusted independent predictors of sICH were increasing age (17 points), higher baseline National Institutes of Health Stroke Scale (42 points), higher systolic blood pressure (21 points), higher blood glucose (8 points), Asian race (9 points), and male sex (4 points). The C-statistic was 0.71 in the derivation sample and 0.70 in the independent internal validation sample. Plots of observed versus predicted sICH showed good model calibration in the derivation and validation cohorts. The model was externally validated in National Institute of Neurological Disorders and Stroke trial patients with a C-statistic of 0.68.

Conclusions—The GWTG-Stroke sICH risk “GRAPS” score provides clinicians with a validated method to determine the risk of sICH in patients treated with intravenous tissue-type plasminogen activator within 3 hours of stroke symptom onset. (*Stroke*. 2012;43:2293-2299.)

| Points for age | |
|--|--------|
| Class | Points |
| ≤ 60 | 8 |
| 61-70 | 11 |
| 71-80 | 15 |
| > 80 | 17 |
| Points for NIHSS | |
| Class | Points |
| 0-5 | 25 |
| 6-10 | 27 |
| 11-15 | 34 |
| 16-20 | 40 |
| > 20 | 42 |
| Points for Systolic Blood Pressure (mm Hg) | |
| Class | Points |
| < 120 | 10 |
| 120-149 | 14 |
| 150-179 | 18 |
| ≥ 180 | 21 |
| Points for Blood Glucose (mg/dL) | |
| Class | Points |
| < 100 | 2 |
| 100-149 | 6 |
| ≥ 150 | 8 |
| Points for Ethnicity | |
| Class | Points |
| Asian | 9 |
| Non-asian | 0 |
| Points for Gender | |
| Class | Points |
| Male | 4 |
| Female | 0 |



Improved Prediction of Poor Outcome After Thrombolysis Using Conservative Definitions of Symptomatic Hemorrhage

Christoph Gumbinger, MD*; Philipp Gruschka, MD*; Markus Böttger, MD; Kristin Heerlein, MD; Robin Barrows, MD; Werner Hacke, MD; Peter Ringleb, MD

Table 2. OR and 95% CI for End points 'Mortality,' 'Favorable Outcome' (mRS 0–2), and 'Unfavorable Outcome' (mRS 3–6), After 3 Months for Different Definitions of sICH and Parenchymal Hemorrhages as Compared With Patients Without Hemorrhage

| Definition | Kappa | OR for Mortality (mRS 0–5 Versus mRS 6; 95% CI) | OR for Unfavorable Outcome (mRS 0–2 Versus mRS 3–6; 95% CI) | Rate of ICH (95% CI) |
|------------|-------|---|---|-------------------------|
| NINDS | 0.57 | 5.67 (2.16–14.72) | 10.42 (2.49–93.06) | 7.7% (4.9%–11.4%) |
| ECASS 2 | 0.85 | 4.67 (1.48–14.33) | 6.82 (1.54–62.21) | 5.4% (3.2%–8.7%) |
| SITS | 0.65 | 14.35 (3.25–85.86) | 8.87 (1.23–387.52) | 3.5% (1.7%–6.3%) |
| ECASS 3 | 0.62 | 12.30 (2.66–75.31) | 7.93 (1.07–350.05) | 3.2% (1.5%–5.8%) |
| PH2 | 0.61 | 3.56 (0.85–13.55) | 4.40 (0.91–41.83) | 3.8% (2.0%–6.7%) |
| PH | 0.61 | 2.96 (1.24–6.80) | 3.67 (1.49–10.28) | 10.9% (7.5%–15.2%) |

mRS indicates modified Rankin Scale; sICH, symptomatic intracerebral hemorrhage; NINDS, National Institute of Neurological Disorders and Stroke; ECASS, European Cooperative Acute Stroke Study; SITS, Safe Implementation of Thrombolysis in Stroke; PH, parenchymal hematoma; OR, odds ratio; CI, confidence interval.

Comparison of Risk-scoring Systems in Predicting Symptomatic Intracerebral Hemorrhage After Intravenous Thrombolysis

Sheng-Feng Sung, MD; Solomon Chih-Cheng Chen, MD, PhD; Huey-Juan Lin, MD, MPH;
Yu-Wei Chen, MD; Mei-Chiun Tseng, PhD; Chih-Hung Chen, MD

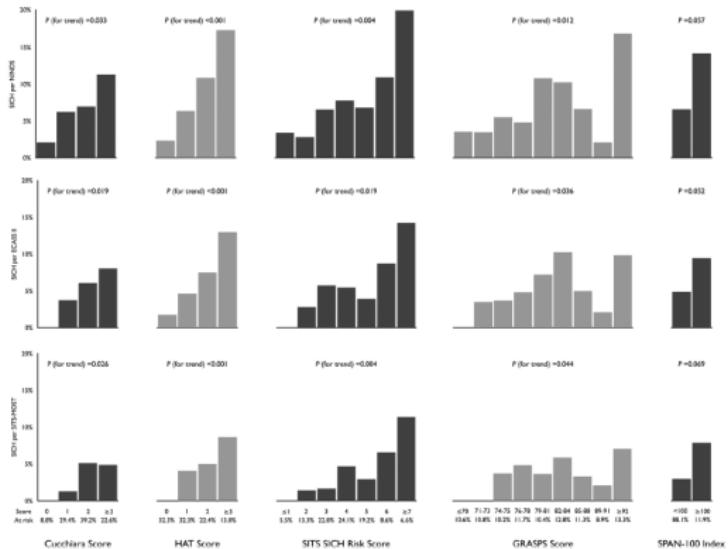


Figure. Observed rate of SICH categorized by various risk score models. At risk means proportion of all thrombolysed patients with the respective risk score. ECASS indicates European-Australasian Cooperative Acute Stroke Study; GRASPS, Glucose Race Age Sex Presure Stroke Severity; NINDS, National Institute of Neurological Disorders and Stroke; SICH, symptomatic intracerebral hemorrhage; and SITS-MOST, Safe Implementation of Thrombolysis in Stroke-Monitoring Study.

Sung S-F. et al Stroke 2013

| Model | Variables used | Cut-off points | Definition of SICH |
|----------------------|---|---|--------------------|
| Cucchiara score | Age NIHSS Glucose Platelet count | >60 y >10 >150 mg/dL <150,000 /mm ³ | NINDS |
| HAT score | NIHSS Glucose Hypodensity on CT History of diabetes | <15, 15-20, >20 >200 mg/dL <1/3 of MCA territory, ≥1/3 of MCA territory | NINDS ^a |
| SITS SICH risk score | Age, NIHSS Glucose SBP Weight OTT Aspirin monotherapy Aspirin + clopidogrel History of hypertension | ≥72 y 7-12, ≥13 ≥180 mg/dL ≥146 mm Hg ≥95 kg ≥180 min | SITS-MOST |
| GRASPS score | Age NIHSS Glucose SBP Ethnicity Gender | ≤60, 61-70, 71-80, >80 y 0-5, 6-10, 11-15, 16-20, >20 <100, 100-149, ≥150 mg/dL <120, 120-149, 150-179, ≥180 mm Hg Non-Asian, Asian | NINDS |
| SPAN-100 index | Age + NIHSS | ≥100 | NINDS |

- ① Is hemorrhagic transformation bad ?
- ② Is hemorrhagic transformation predictable ?

- ① Is hemorrhagic transformation bad ?
- ② Is hemorrhagic transformation predictable ?
- ③ How to manage patients with hemorrhagic transformation ?

Management of hemorrhagic transformation

No proven protocol

- Prevention
- Detection
- Treatment

Management of hemorrhagic transformation

No proven protocol

- Prevention
 - BP control before, during, and after IV thrombolysis
- Detection
- Treatment

Management of hemorrhagic transformation

No proven protocol

- Prevention
 - BP control before, during, and after IV thrombolysis
 - Avoidance of anti-thrombotics within 24 hours of IV thrombolysis
- Detection
- Treatment

Management of hemorrhagic transformation

No proven protocol

- Prevention
 - BP control before, during, and after IV thrombolysis
 - Avoidance of anti-thrombotics within 24 hours of IV thrombolysis
- Detection
 - Predictors and Risk scores
 - Non-contrast CT or MR
- Treatment

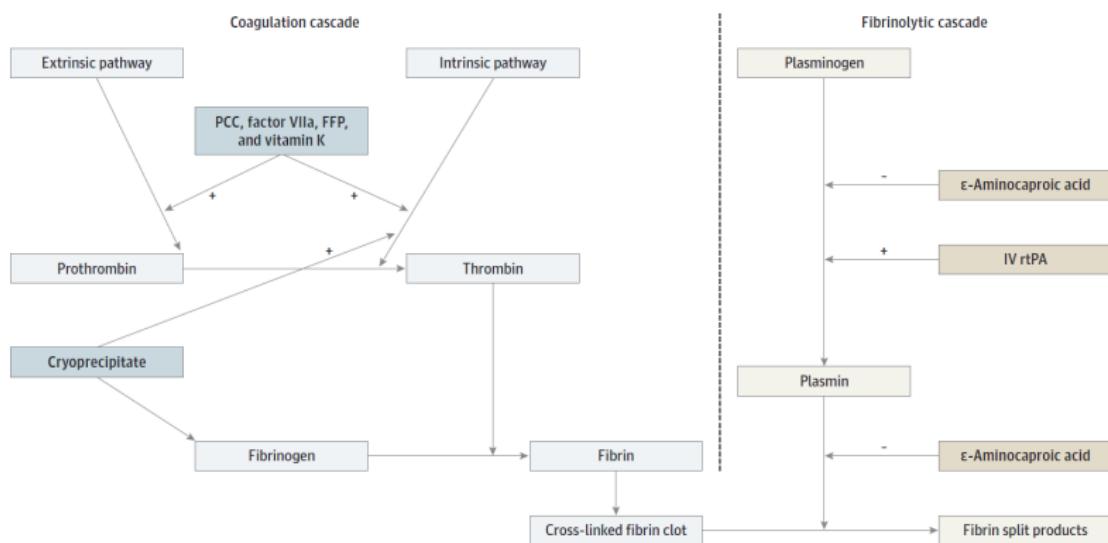
In case of symptomatic parenchymal hematoma,

- CBC, coagulation parameters (PT, aPTT), and fibrinogen levels
- Cryoprecipitate, FFP, Platelet
- Tranexamic acid ?
- Hematoma evacuation ?
- BP control ?

Table 4. Clinical Management of sICH

| Patient Age, y/Sex | Intervention | Laboratory Values | | | Therapy | ICH Volume, mL | Change in Volume, % | Outcome |
|--------------------|--------------|-------------------|-------------------|--|---|----------------|---------------------|---------|
| | | D-Dimer, µg/mL | Fibrinogen, mg/dL | | | | | |
| 89/M | IV | 8.6 | 417 | | Phytonadione ^a | 31.3 | 36.9 | Death |
| 88/M | IV | NM | NM | | None | 153.8 | ND | Death |
| 80/F | IV | NM | NM | | None | 105.8 | ND | Death |
| 56/M | IV | 6.6 | 288 | | None | 15.7 | 64.1 | Death |
| 78/M | IAT | NM | 286 | | FFP ^b | 140.3 | 1.4 | Death |
| 91/M | IV | 2.8 | 132 | | None | 103.6 | ND | Death |
| 77/M | IV | NM | 377 | | Cryo | 81.1 | ND | Rehab |
| 53/M | IV | 3.0 | 249 | | FFP, cryo, and platelets | 9.0 | -1.0 | Rehab |
| 71/M | IV | 7.3 | 291 | | FFP, cryo, and platelets | 53.7 | 39.7 | Death |
| 92/F | IV | NM | NM | | Phytonadione ^a | 9.3 | 6.3 | Death |
| 72/M | IV | 4.5 | 284 | | FFP and phytonadione ^{a,b} | 43.7 | ND | Death |
| 86/M | IV | NM | 194 | | None | 8.8 | ND | Death |
| 89/F | IV | 2.8 | 301 | | Cryo | 9.8 | 45.7 | Death |
| 75/F | IV | 8.2 | 282 | | FFP, cryo, aminocaproic acid, and platelets | 131.6 | ND | Death |
| 81/F | IV | 8.6 | 315 | | None | 169.0 | 6.8 | Death |
| 79/F | IV | NM | NM | | None ^b | 9.5 | ND | Rehab |
| 84/F | IV | 5.2 | 164 | | None | 41.1 | -2.4 | Home |
| 89/F | IV + IAT | NM | NM | | FFP and phytonadione ^a | 132.4 | ND | Death |
| 24/F | IV | 1.7 | | | None | 8.8 | -1.1 | Death |
| 58/M | IV | 1.7 | 115 | | FFP ^b | 49.3 | ND | Rehab |

Figure. Coagulation and Fibrinolytic Pathways Showing the Mode of Action of Symptomatic Intracerebral Hemorrhage Treatment



FFP indicates fresh frozen plasma; IV, intravenous; PCC, prothrombin complex concentrate; rtPA, recombinant tissue plasminogen activator; +, activation; and -, inhibition. Treatments are indicated with boldface type.

PRACTICAL PEARL

Treatment of Intracerebral Hemorrhage with Tranexamic Acid After Thrombolysis with Tissue Plasminogen Activator

K. F. French · Jacob White · R. E. Hoesch

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Abstract

Background Thrombolytic treatment with intravenous tissue plasminogen activator (iv tPA) is the only FDA-approved therapy for acute ischemic stroke. There are risks associated with thrombolytics, including intracranial and extracranial hemorrhage and hypersensitivity reactions. Established treatment for post-tPA hemorrhage includes administration of blood products including cryoprecipitate, fresh frozen plasma, and platelets which have poorly established efficacy. Tranexamic acid (TXA) and epsilon-aminocaproic acid (EACA) have been studied as hemostatic therapies in post-operative hemorrhage, menorrhagia, intracranial hemorrhage (ICH), subarachnoid hemorrhage, and trauma patients. There is no reported literature on the use of TXA to reverse thrombolytic therapy with tPA.

Methods This is a case report of a Jehovah's Witness patient who was unwilling to receive blood products after developing symptomatic ICH following iv tPA. He

consequently received TXA for reversal of thrombolytic therapy.

Results The patient received a total of 1.675 g of iv TXA within 3 h of finishing the iv tPA. Repeat brain imaging with computed tomography and magnetic resonance imaging revealed no further expansion of hemorrhages.

Conclusion TXA is an inexpensive medication which competitively inhibits the activation of plasminogen and can be given to reverse thrombolysis in the setting of hemorrhage after iv thrombolytic therapy.

Keywords Critical care · All cerebrovascular disease/stroke · Infarction · Thrombolysis · Intracerebral hemorrhage

Introduction

Intensive BP lowering in ICH

Table 2. Medical management of ICH

| Component | Recommendation |
|-------------------------------------|--|
| Blood pressure | For patients with SBP > 150 mmHg and ≤ 220 mmHg, early intensive BP-lowering treatment with a target of 140 mmHg can be a safe and effective method. For patients with SBP > 220 mmHg, aggressive BP reduction with a continuous intravenous infusion of BP lowering drugs, such as nicardipine, should be considered. |
| Anticoagulation-related ICH | Withhold anticoagulants and correct INR, if elevated, by intravenous infusion of vitamin K and FFP. PCCs can be considered rather than FFP given its fewer complications and ability to rapidly correct the INR. |
| Antiplatelet medication-related ICH | Consider platelet transfusions, although the evidence is unclear. |
| Thromboprophylaxis | Apply intermittent pneumatic compression at admission to prevent venous thromboembolism. Low-molecular-weight heparin or unfractionated heparin can be applied after cessation of bleeding in immobile patients. Systemic anticoagulation or IVC filter can be considered in patients with symptomatic DVT or pulmonary thromboembolism. |
| ICP | Patients with decreased level of consciousness can be treated by ventricular drainage of the hydrocephalus, if needed. |
| Fever | Hypertonic saline or mannitol can be used appropriately. Fever should be treated with antipyretic medication and/or external or internal cooling methods to prevent poor outcomes. |
| Glucose | Regular monitoring and control of glucose is essential to prevent both hyperglycemia and hypoglycemia. |
| Seizure | Clinical seizures are frequent among patients with ICH and should be treated. Electrographic seizures with decreased level of consciousness should be treated. Continuous EEG monitoring can be beneficial in patients with depressed mental status that is not explainable by hemorrhage. |

SBP, systolic blood pressure; INR, international normalized ratio; FFP, fresh frozen plasma; PCCs, prothrombin complex concentrates; IVC, inferior vena cava; DVT, deep vein thrombosis; ICP, intracranial pressure; ICH, intracerebral hemorrhage; EEG, electroencephalography.

Intensive BP lowering in ICH

INTERACT-II



ATACH-II



0% 20% 40% 60% 80% 100%

BP lowering in Hyperperfusion syndrome after CAS

1598 Abou-Chebl et al.
Hyperperfusion Syndrome Following Carotid Stenting

JACC Vol. 43, No. 9, 2004
May 5, 2004:1596–601

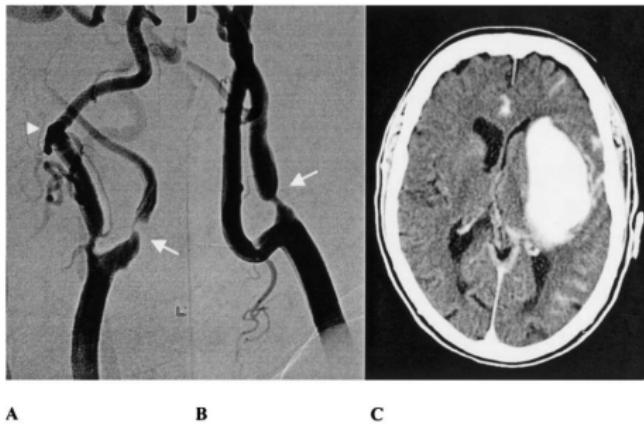


Figure 1. Preoperative angiograms (A and B) from Patient 1 show a 99% stenosis of the left internal carotid artery (ICA) (arrow in A) with delayed filling of the ICA compared with the external carotid artery (arrowhead in A) as well as an 80% stenosis of the origin of the right ICA (arrow in B). Computerized tomography scan of the brain (C) performed 1 h following left carotid stenting shows a large basal ganglia hemorrhage with mild subarachnoid hemorrhage.

Abou-Chebl A. et al JACC 2004

Take-Home Message

- Hemorrhagic transformation is not rare in patients with acute ischemic stroke.
- Especially, parenchymal hematoma type II might be the marker of worse outcome
- More attention should be paid to patients of old age, with large infarction volume, and CE.
- Standard treatment guideline for hemorrhagic transformation does not exist.