

## 2017 SNUH International Stroke Symposium

# Hemorrhagic Transformation in Ischemic Stroke



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## ① Is hemorrhagic transformation bad ?

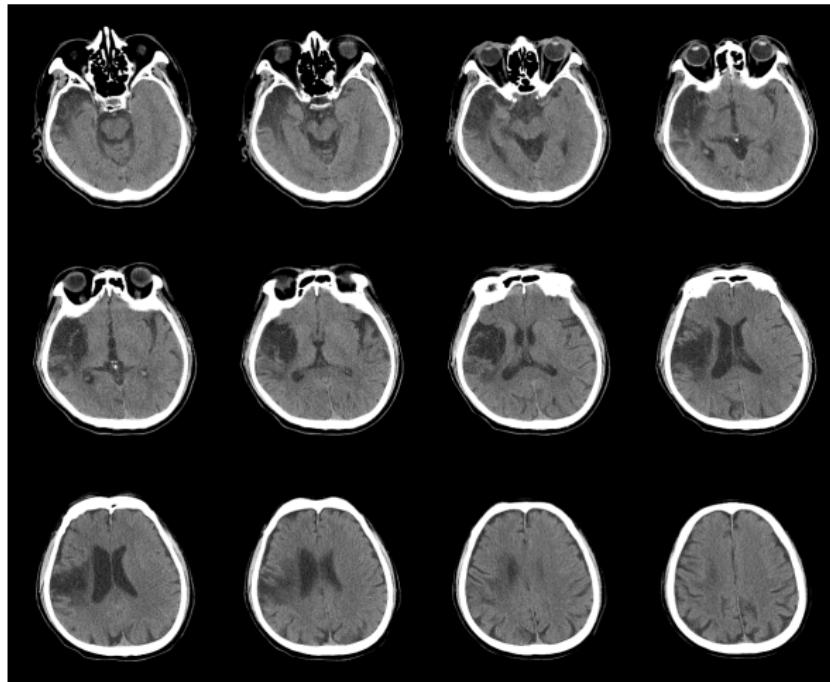
**Table 3.** Distribution of different types of HT related to early improvement/deterioration and tPA treatment

	Non-tPA	tPA	Total
<i>Deterioration &gt;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 &gt;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.

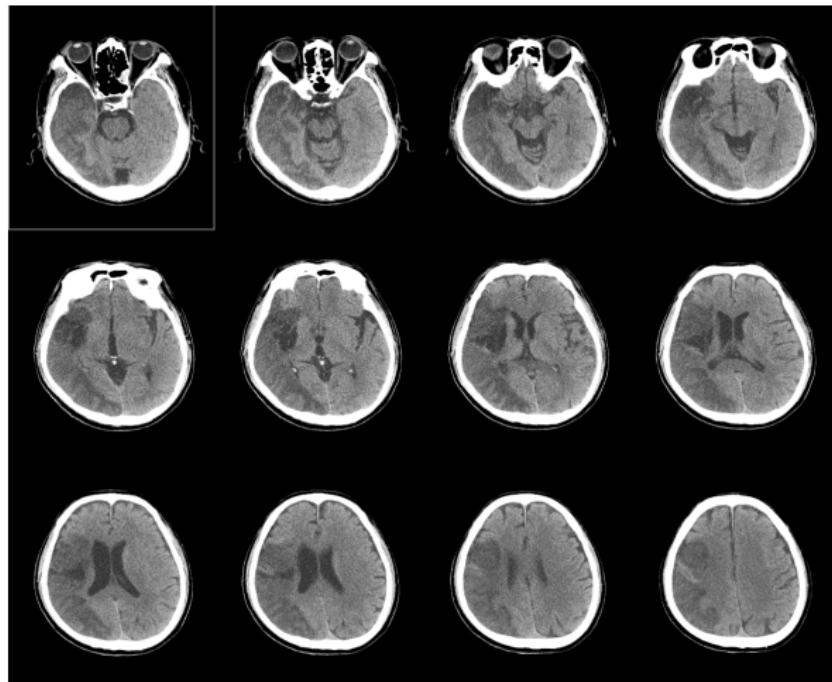
Among 122 consecutive stroke patients (mean age 65.5 years), 19 patients (15.6%) showed early improvement which was associated with the occurrence of Hemorrhagic Transformation ( $p = 0.011$ ) and tPA treatment ( $p < 0.001$ )

68YO Male with Lt. distal ICA occlusion



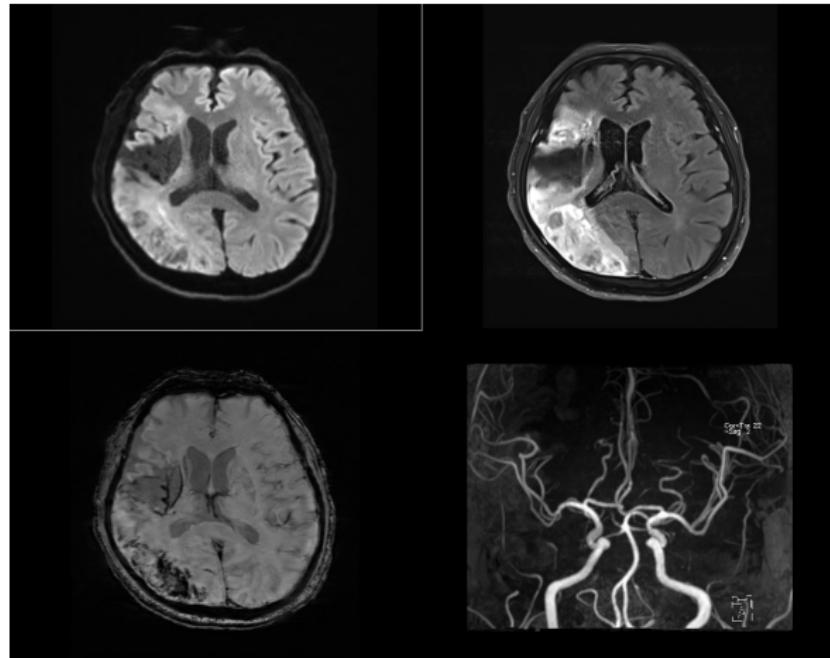
NIHSS 9: Facial palsy 1, LU 2, LL 2, Seosory 2, Dysarthria 1, Neglect 2

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

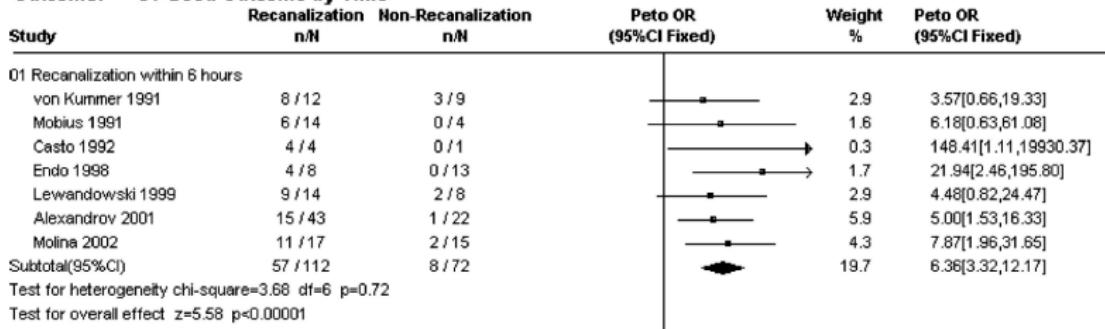
# The Impact of Recanalization on Ischemic Stroke Outcome

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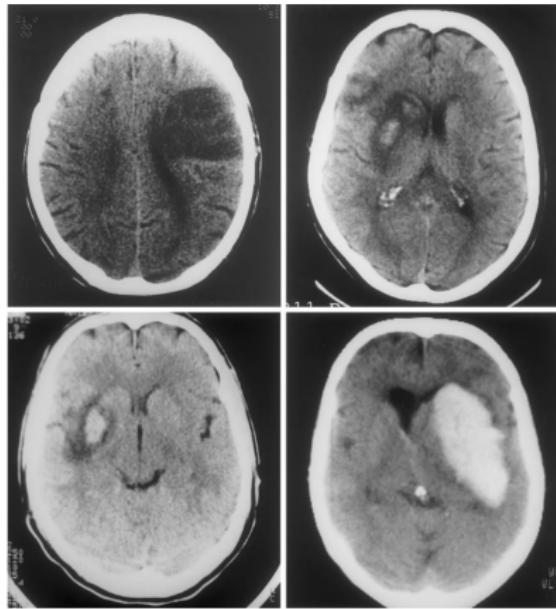
- 1 Definition
- 2 Prevalence
- 3 Prognosis
- 4 Predictors
- 5 Management
- 6 Summary

# 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.

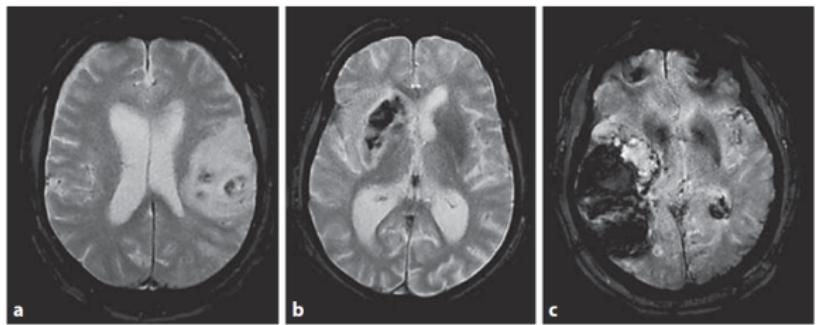
Fiorelli M. et al. Stroke. 1999;30:2280-2284

# Imaging definition



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

# Imaging definition



**Fig. 1.** The three categories of HT on T<sub>2</sub>\*-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  $\geq 4$  within 7 days of onset (ECASS II)
- NIHSS score aggravation  $\geq 4$  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

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ECASS 3	Any hemorrhage with neurologic deterioration as indicated by an NIHSS score that was higher by $\geq 4$ 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 $\geq 4$ 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 $\geq 4$ 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

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# 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 <sup>a</sup>
<b>IV FIBRINOLYSIS</b>						
NINDS	312	7–10 days	4.5% (14/312)	6.4% (20/312)	N/A	1.5 h <sup>b</sup>
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 <sup>b</sup>
SITS-MOST	6483	22–36 h	9.6% (617/6483)	7.3% (468/6483)	2.9% (184/6352)	2.3 h <sup>b</sup>
ECASS-III	418	36 h	27% (113/418)	2.4% (10/418)	1.9% (8/418)	3.98 h <sup>b</sup>
IST-III	1515	7 days	N/A	6.9% (104/1515)	N/A	4.2 h <sup>b</sup>
<b>IA FIBRINOLYSIS</b>						
PROACTI	26	90 days	50% (13/26)	15.4% (4/26)	7.7% (2/26)	5.5 h <sup>b</sup>
PROACTII	121	7–10 days	68% (73/108)	10% (11/108)	N/A	4.5 h <sup>b</sup>
<b>COMBINED IV/IA APPROACH</b>						
EMS	17	7 ± 1 days	11.8% (2/17)	23.5% (4/17)	0.0% (0/17)	2.6 h <sup>b</sup> /6.3 h <sup>d</sup>
IMS-I	80	36 h	43% (34/80)	6.3% (5/80)	7.5% (6/80)	1.33 h <sup>b</sup> /3.53 h <sup>d</sup>
IMS-II	81	36 h	32.1% (26/81)	9.9% (8/81)	8.6% (7/81)	2.37 h <sup>b</sup> /N/A <sup>d</sup>
IMS-III	434	24 ± 6 h	27.4% (119/434)	6.2% (27/434)	5.8% (25/434)	2.03 h <sup>b</sup> /N/A <sup>d</sup>
<b>MECHANICAL THROMBECTOMY</b>						
Merci						
Phase I	28	24 h	42.9% (12/28)	0.0% (0/28)	0.0% (0/28)	6.25 h <sup>d</sup>
MERCI Trial	141	24 h	27.7% (39/141)	78% (111/141)	1.4% (2/141)	6.4 h <sup>b,d</sup>
Multi-MERCI	164	24 h	30.5% (50/164)	9.8% (16/164)	2.4% (4/164)	5.9 h <sup>b,d</sup>
Penumbra						
Pivotal Stroke Trial	125	24 h	16.8% (21/125)	11.2% (14/125)	1.6% (2/125)	4.85 h <sup>d</sup>
POST Trial	157	24 h	13.4% (21/157)	6.4% (10/157)	N/A	5.18 h <sup>d</sup>
Solitaire						
Phase I	20	24 h	30% (6/20)	10.0% (2/20)	5.0% (1/20)	6.7 h <sup>d</sup>
SWIFT Trial	58	24 h	15.5% (9/58)	2.0% (1/58)	0.0% (0/58)	5.54 h <sup>b,d</sup>
Trevo						
TREVO	60	N/A	N/A	N/A	N/A	5.03 h <sup>d</sup>
TREVO-2	88	18–36 h	40.9% (36/88)	4.5% (4/88)	8.0% (7/88)	5.4 h <sup>b,d</sup>

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  $5 \pm 2$  after stroke onset. Study outcomes were 3-month mortality or disability. Disability was assessed using a modified Rankin score ( $\geq 3$  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  $\chi^2$  test. Multiple logistic regression analysis was used to identify predictors for HT.

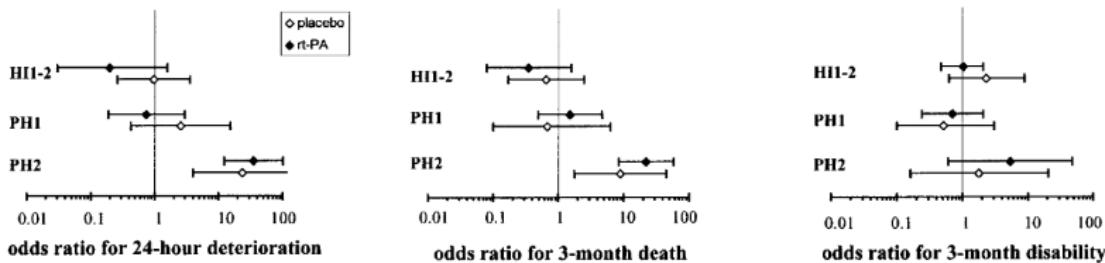
**Results**—Among 1125 consecutive patients (median age 76.00 years), 98 (8.7%) had HT, 62 (5.5%) had hemorrhagic infarction, and 36 (3.2%) parenchymal hematoma. At 3 months, 455 patients (40.7%) were disabled or died. Death or disability was seen in 33 patients with parenchymal hematoma (91.7%), in 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

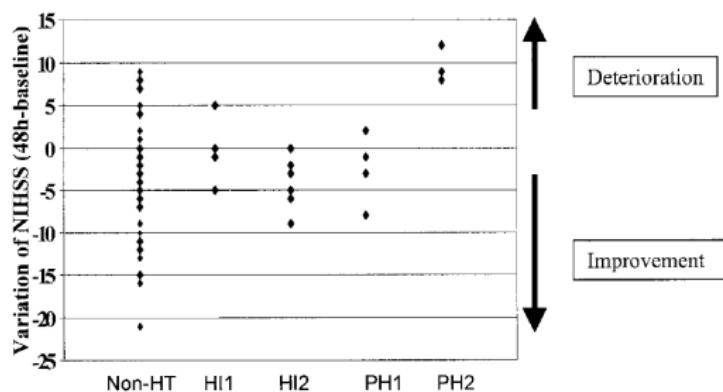
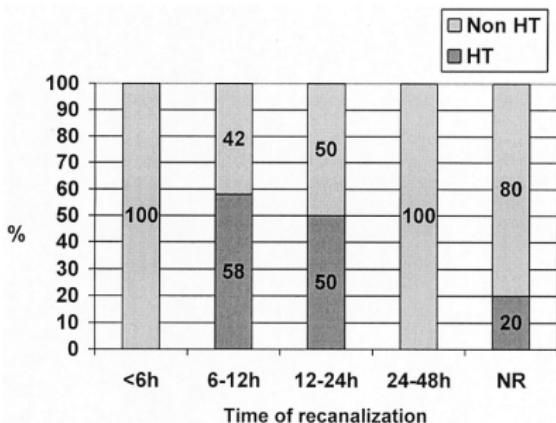


**Figure 3.** ORs and 95% CIs for 24-hour deterioration (decrease of the NIHSS score of  $\geq 4$  points compared with baseline), 3-month death, and 3-month disability (Rankin scale score of  $\geq 2$ ) in placebo and rtPA arms. ORs are adjusted for age and extent of early signs of infarct on baseline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

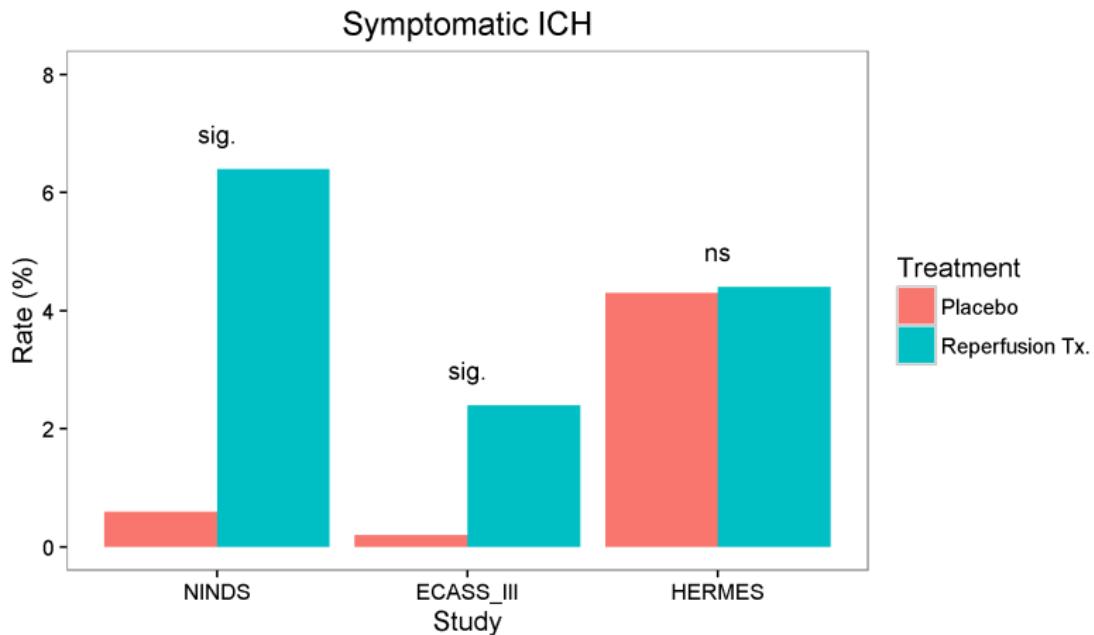
Paciaroni M. et al. Stroke 2008

# 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

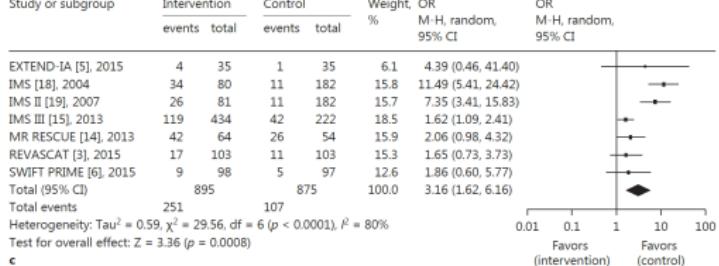
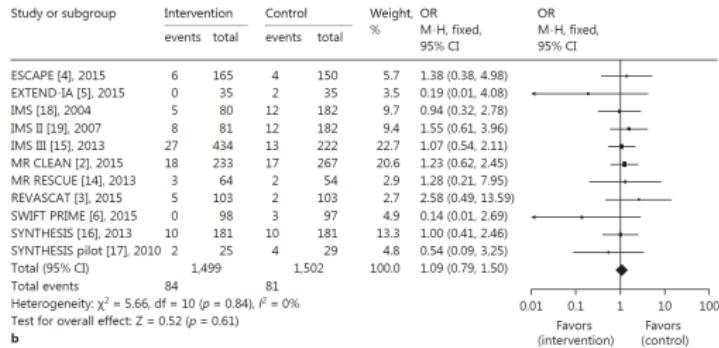
Mazya M. et al Stroke 2012; Larrue V. et al Stroke 2001; Paciaroni M. et al Stroke 2008; Kim BJ et al Stroke 2009; Jauch E.C. et al Stroke 2013; Zhang J et al Ann Transl Med 2014

# Reperfusion therapy

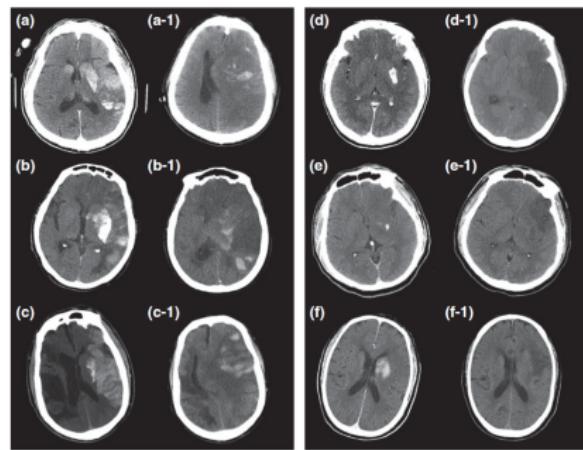


NINDS study group NEJM 1995; Hacke W et al. NEJM 2008; Goyal M et al. Lancet 2016

## Symptomatic (b) and asymptomatic (c) hemorrhagic transformation



# Cortical enhancement on CT



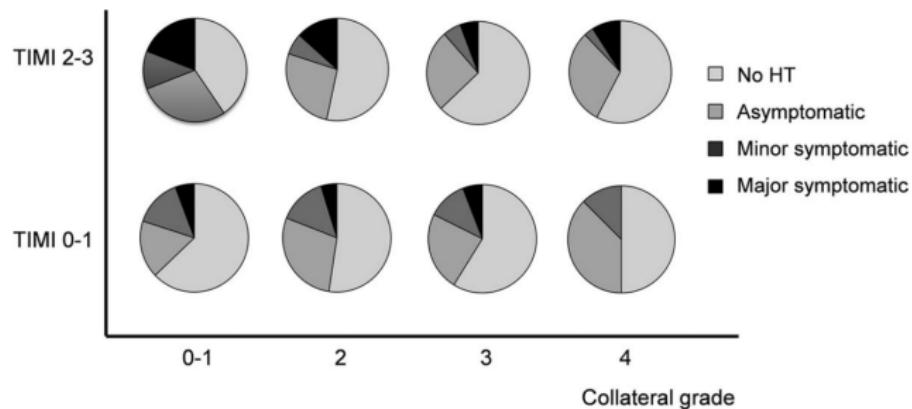
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Sensitivity	93%
Specificity	52%
Positive predictive value	39%
Negative predictive value	96%

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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

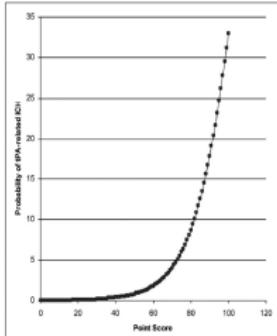
**Background and Purpose**—There are few validated models for prediction of risk of symptomatic intracranial hemorrhage (sICH) after intravenous tissue-type plasminogen activator treatment for ischemic stroke. We used data from Get With The Guidelines—Stroke (GWTG-Stroke) to derive and validate a prediction 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  $\beta$  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
$\leq 60$	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
$\geq 180$	21
Points for Blood Glucose (mg/dL)	
Class	Points
$< 100$	2
100-149	6
$\geq 150$	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

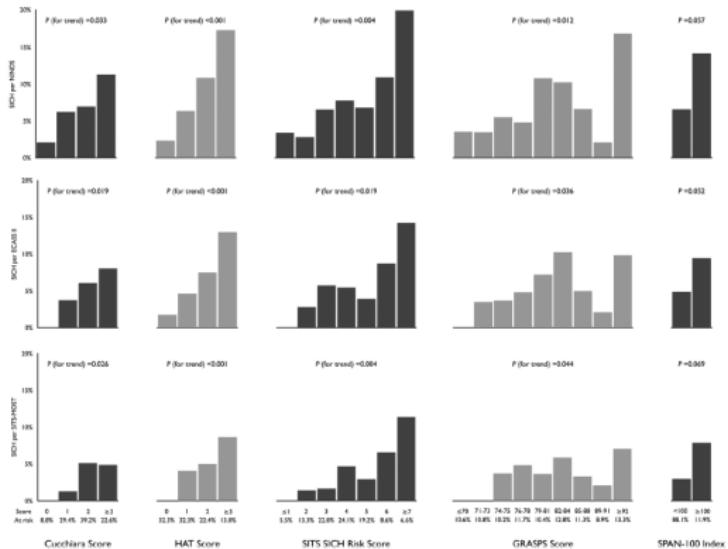


Figure. Observed rate of SICH categorized by various risk score models. At risk means proportion of all thrombolysed patients with the respective risk score. ECASS indicates European-Australasian Cooperative Acute Stroke Study; GRASPS, Glucose Race Age Sex Presure Stroke Severity; NINDS, National Institute 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 <sup>3</sup>	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 <sup>a</sup>
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 ?
- 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 <sup>a</sup>	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 <sup>b</sup>	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 <sup>a</sup>	9.3	6.3	Death
72/M	IV	4.5	284		FFP and phytonadione <sup>a,b</sup>	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 <sup>b</sup>	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 <sup>a</sup>	132.4	ND	Death
24/F	IV	1.7			None	8.8	-1.1	Death
58/M	IV	1.7	115		FFP <sup>b</sup>	49.3	ND	Rehab

## PRACTICAL PEARL

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

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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

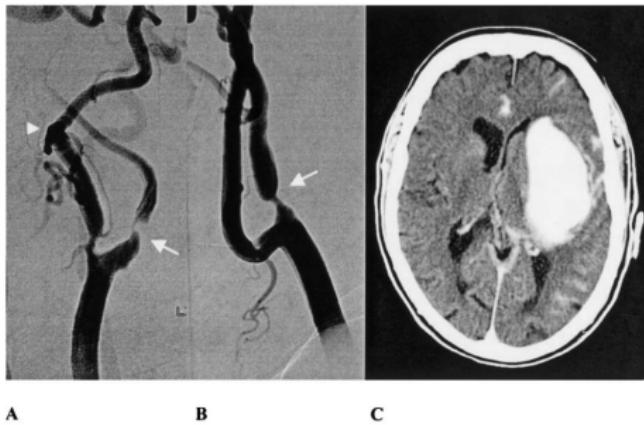
Component	Recommendation
Blood pressure	For patients with SBP > 150 mmHg and ≤ 220 mmHg, early intensive BP-lowering treatment with a target of 140 mmHg can be a safe and effective method. For patients with SBP > 220 mmHg, aggressive BP reduction with a continuous intravenous infusion of BP lowering 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.

# 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 subtype might be the marker of worse outcome
- More attention should be paid to patients of old age, with large infarction volume, and CE. In addition, cortical enhancement after IA thrombectomy might be used as screening marker.
- Standard treatment guideline for hemorrhagic transformation does not exist.