TIMING OF ANTIPLATELET POST RTPA

OUTLINE

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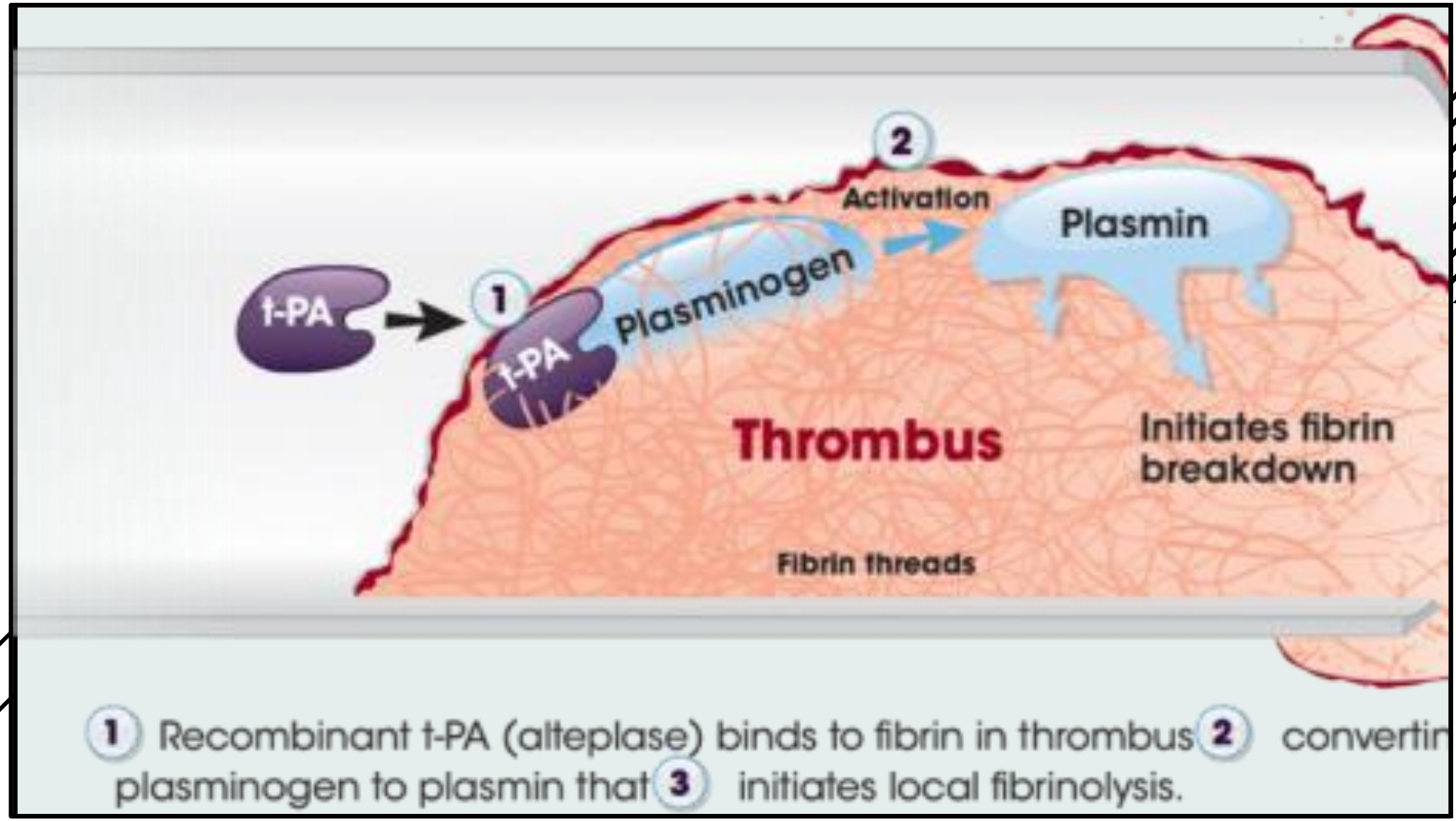
Introduction

- IV alteplase is the first thrombolytic drug recommended in acute ischemic stroke as AHA guideline(IA).
- Alteplase is a fibrinolytic agent; also referred to as tissue plasminogen activator (tPA).
- For those treated with IV alteplase, aspirin administration is generally **delayed until 24 hours** later but **might be considered** in the presence of concomitant conditions for which such treatment given in the absence of IV alteplase is **known to provide substantial benefit** or **withholding cause substantial risk**.

Mechanism of TPA

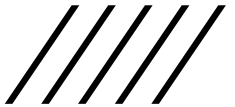
- Alteplase converts plasminogen to the proteolytic enzyme plasmin, which lyses fibrin as well as fibrinogen.
- Intravenous bolus in cases of stroke, the activity of tPA is not limited to plasminogen activation on fibrin matrices. At therapeutic concentrations, tPA can drive plasminogen activation when bound to circulating fibrinogen, thus mediating fibrinogenolysis, which results in fibrinogen consumption and reduced hemostatic potential.
- Intravenous alteplase is cleared primarily by the liver with an initial half-life of fewer than 5 minutes and a **terminal half-life of 72 minutes**.



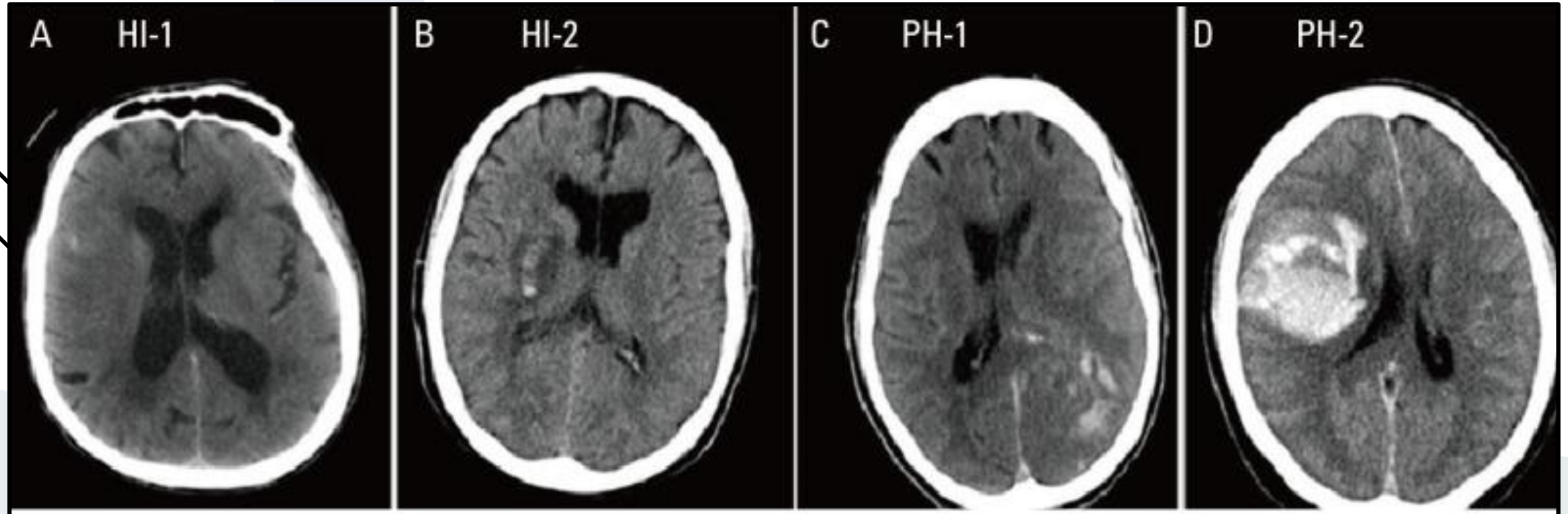
1 Recombinant t-PA (alteplase) binds to fibrin in thrombus 2 convertin
plasminogen to plasmin that 3 initiates local fibrinolysis.

Risk factors of post TPA bleeding

- The natural of AIS by itself is associated with hemorrhagic transformation.
- ICH can be defined clinically (symptomatic vs. asymptomatic), radiologically (HI-1, HI-2, PH-1, PH-2).
- sICH is defined as a worsening of NIHSS by ≥4 points within the first 36 h of stroke onset that is attributable to Hemorrhagic transformation.
- Asymptomatic ICH usually involves HI lesions as opposed to PH lesions, without any impact on 3 months functional outcome.



Front Neurol. 2021 May 14;12:661955.



A	Hemorrhagic infarction - 1	Isolated petechial staining of infarcted tissue without mass effect
B	Hemorrhagic infarction - 2	Onfluent patechiae in infarcted tissue without mass effect
C	Parenchymal Hemorrhage - 1	Homogeneous high attenuation lesion with minimal mass effect occupying less than 30% of the infarcted area
D	Parenchymal Hemorrhage - 2	Lesion occupying more than 30% of the infarcted area with definite mass effect

Risk factors of post TPA bleeding

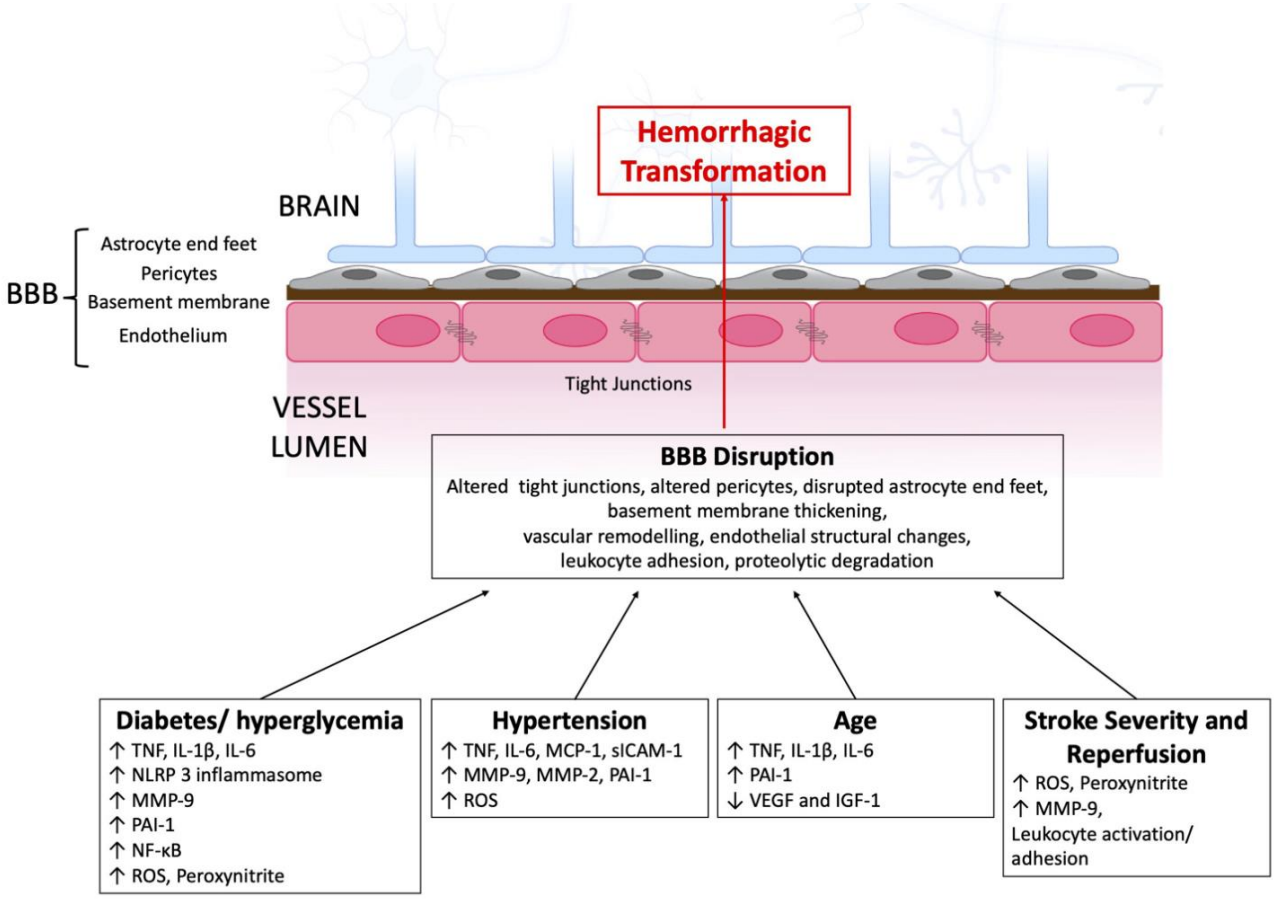


FIGURE 1 | Immune pathways contributing to BBB disruption and subsequent HT after AIS. BBB, blood-brain barrier; IGF-1, insulin-like growth factor 1IL, interleukin; MCP-1, monocyte chemoattractant protein 1; MMP, matrix metalloproteinase; NF-κB, nuclear factor-κB; NLRP3, NOD-, LRR- and pyrin domain-containing protein 3; PAI-1, plasminogen activator inhibitor-1; ROS, reactive oxygen species; TLR, toll like receptor; TNF, tumor necrosis factor; VEGF, vascular endothelial growth factor.

- Clinical features associated with an increased risk of HT in patients with ischemic stroke include stroke severity (NIHSS), hypertension, hyperglycemia, poor collaterals, low platelet count, use of antithrombotic drugs, and reperfusion therapy.

Front Neurol. 2021 May 14;12:661955.

Risk factors of post TPA bleeding

- In the ECASS 3 trial, the frequency of any ICH in the placebo group reached 17.6%, with 3.5% being sICH.
- Treatment with alteplase is associated with a 6–8% risk of sICH.
- This is mediated in that thrombolytics breakdown blood clots and recanalize occluded cerebral vasculature, which can promote BBB disruption, contributing to reperfusion injury and increased risk of HT.
- Activation of platelets, coagulation factors, and the innate and adaptive immune systems also contribute to injury following restoration of blood flow.

Risk factors of post TPA bleeding

- Meta-analysis analyzed risk of ICH after alteplase in acute ischemic stroke, 6756 participants in the nine trials of intravenous alteplase versus control were included.
- The results showed
  - type 2 PH: 231 [6·8%] of 3391 *vs* 44 [1·3%] of 3365; OR 5·55, 95% CI 4·01–7·70; **absolute excess 5·5%** [4·6–6·4]
  - type 2 PH with an increase in NIHSS of 4 points or more or that led to death within 36 h of treatment 124 [3·7%] of 3391 *vs* 19 [0·6%] of 3365; OR 6·67, 4·11–10·84; **absolute excess 3·1%** [2·4–3·8]
  - fatal intracerebral haemorrhage within 7 days: 91 [2·7%] of 3391 *vs* 13 [0·4%] of 3365; OR 7·14, 3·98–12·79; **absolute excess 2·3%** [1·7–2·9%]

Lancet Neurol. 2016 Aug;15(9):925-933.

Risk factors of post TPA bleeding

- Pool analysis from SAINT I and SAINT II trials, compared patients received tpa within 3 hours and placebo, showed sICH in thrombolytic group associated with prior stroke, baseline antiplatelet use, higher NIHSS and ASPECT ≤7

Table 2. Multivariable Logistic Regression Model for sICH Versus No ICH

Factor	OR (95% CI)	*P*
Age per year	1.02 (0.99–1.05)	0.17
Smoking	0.49 (0.18–1.36)	0.17
Prior stroke	0.13 (0.03–0.60)	0.009
Antiplatelet therapy		
Single	2.04 (1.07–3.87)	0.03
Double	9.29 (3.28–26.32)	<0.001
NIHSS per point	1.09 (1.03–1.15)	0.002
ASPECTS		
8–9	2.26 (0.63–8.10)	0.21
≤7	5.63 (1.66–19.10)	0.006

Note. Analysis incorporated all factors significant in univariable analysis at $P<0.10$. N=784.

Stroke. 2009;40:3067-3072.

Risk factors of post TPA bleeding

- Study from China, **prior stroke and atrial fibrillation** are associated with ICH after thrombolysis, OR 5.752 (95% CI 1.487–22.248; *P*=0.011) and OR 5.428 (95% CI: 1.427–20.64; *P* = 0.013) respectively.

Table 2. Multivariable logistic regression for early ICH

	Unadjusted	
	OR (95% CI)	*P* value
Prior stroke	3.995 (1.179-13.534)	0.026*
Atrial fibrillation	3.404 (1.048-11.062)	0.042*
	Adjusted†	
	OR (95% CI)	*P* value
Prior stroke	5.752 (1.487-22.248)	0.011*
Atrial fibrillation	5.428 (1.427-20.640)	0.013*
Age	0.968 (0.918-1.021)	0.230
Sex	3.080 (0.869-10.910)	0.081
Blood glucose	1.058 (0.897-1.247)	0.503
admission NIHSS score	0.969 (0.877-1.070)	0.532

OR, odds ratio; CI, confidence interval.
†Adjusted for age, sex, blood glucose, and admission NIHSS score.
*$P<0.05$

J Atheroscler Thromb, 2020; 27: 1176-1182.

Risk factors of post TPA bleeding

	NINDS A[11]	NINDS B[11]	ECASS I[8]	ECASS II[12]	ATLANTIS A[15]	ATLANTIS B[14]	ECASS III[13]	EPITHET[10]	IST-3[9]	Total
Patients	291	333	620	800	142	613	821	101	3035	6756
Alteplase	144 (49%)	168 (50%)	313 (50%)	409 (51%)	71 (50%)	301 (49%)	418 (51%)	52 (51%)	1515 (50%)	3391 (50%)
Control	147 (51%)	165 (50%)	307 (50%)	391 (49%)	71 (50%)	312 (51%)	403 (49%)	49 (49%)	1520 (50%)	3365 (50%)
Treatment delay (h)	2·0 (0·6)	2·0 (0·6)	4·4 (1·1)	4·3 (1·1)	4·3 (1·1)	4·4 (0·8)	4·0 (0·4)	4·9 (0·8)	4·2 (1·2)	4·0 (1·2)
>0 to ≤3	290 (>99%)	333 (100%)	87 (14%)	158 (20%)	22 (15%)	39 (6%)	..	..	620 (20%)	1549 (23%)
>3 to ≤4·5	1 (<1%)	..	233 (38%)	265 (33%)	53 (37%)	249 (41%)	788 (96%)	31 (31%)	1148 (38%)	2768 (41%)
>4·5	..	..	295 (48%)	370 (46%)	67 (47%)	321 (52%)	6 (1%)	69 (68%)	1266 (42%)	2394 (35%)
Missing	..	..	5 (1%)	7 (1%)	..	4 (1%)	27 (3%)	1 (1%)	1 (<1%)	45 (1%)
Age (years)	66 (11)	68 (12)	65 (12)	66 (11)	66 (13)	66 (11)	65 (12)	72 (13)	77 (12)	71 (13)
≤80	279 (96%)	289 (87%)	615 (>99%)	792 (99%)	142 (100%)	608 (>99%)	805 (98%)	76 (75%)	1418 (47%)	5024 (74%)
>80	12 (4%)	44 (13%)	5 (1%)	8 (1%)	..	3 (<1%)	15 (2%)	25 (25%)	1617 (53%)	1729 (26%)
Missing	..	..	..	..	..	2 (<1%)	1 (<1%)	..	..	3 (<1%)
Stroke severity (NIHSS)	14 (7)	15 (7)	12 (6)	12 (6)	13 (7)	11 (6)	10 (5)	13 (6)	12 (7)	12 (7)
>0 to ≤4	16 (5%)	13 (4%)	34 (5%)	47 (6%)	10 (7%)	47 (8%)	98 (12%)	1 (1%)	400 (13%)	666 (10%)
>4 to ≤10	78 (27%)	98 (29%)	189 (30%)	339 (42%)	57 (40%)	279 (46%)	389 (47%)	40 (40%)	1064 (35%)	2533 (37%)
>10 to ≤15	68 (23%)	63 (19%)	183 (30%)	232 (29%)	28 (20%)	128 (21%)	163 (20%)	22 (22%)	601 (20%)	1488 (22%)
>15 to ≤21	76 (26%)	78 (23%)	146 (24%)	113 (14%)	25 (18%)	106 (17%)	142 (17%)	29 (29%)	618 (20%)	1333 (20%)
>21	45 (15%)	74 (22%)	28 (5%)	43 (5%)	20 (14%)	33 (5%)	18 (2%)	9 (9%)	352 (12%)	622 (9%)
Missing	8 (3%)	7 (2%)	40 (6%)	26 (3%)	2 (1%)	20 (3%)	11 (1%)	..	..*	114 (2%)
Women	120 (41%)	142 (43%)	231 (37%)	331 (41%)	45 (32%)	250 (41%)	325 (40%)	43 (43%)	1570 (52%)	3057 (45%)
History of hypertension	188 (65%)	220 (66%)	258 (42%)	412 (52%)	87 (61%)	364 (59%)	514 (63%)	71 (70%)	1954 (64%)	4068 (60%)
History of stroke	49 (17%)	34 (10%)	83 (13%)	158 (20%)	31 (22%)	89 (15%)	89 (11%)	11 (11%)	699 (23%)	1243 (18%)
History of diabetes mellitus	64 (22%)	67 (20%)	81 (13%)	169 (21%)	27 (19%)	130 (21%)	129 (16%)	23 (23%)	388 (13%)	1078 (16%)
History of atrial fibrillation	55 (19%)	60 (18%)	113 (18%)	188 (24%)	37 (26%)	97 (16%)	108 (13%)	42 (42%)	914 (30%)	1614 (24%)
Antiplatelet use	78 (27%)	93 (28%)	87 (14%)	196 (25%)	59 (42%)	211 (34%)	201 (24%)	30 (30%)	1306 (43%)	2261 (33%)
Weight (kg)	78 (17)	78 (19)	74 (12)	75 (14)	80 (20)	79 (18)	78 (15)	75 (19)	72 (15)	75 (16)
Systolic blood pressure (mm Hg)	154 (21)	152 (21)	154 (23)	152 (21)	152 (24)	152 (21)	153 (21)	148 (19)	155 (24)	154 (22)
Diastolic blood pressure (mm Hg)	85 (13)	85 (14)	87 (13)	84 (13)	81 (14)	82 (14)	84 (14)	78 (13)	82 (15)	83 (14)

Data are n (%) or mean (SD). NINDS=National Institute of Neurological Disorders and Stroke. ECASS=European Cooperative Acute Stroke Study. ATLANTIS=Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke. EPITHET=Echoplanar Imaging Thrombolytic Evaluation Trial. IST=International Stroke Trial. NIHSS=National Institutes of Health Stroke Scale. *In IST-3, 244 patients had their baseline NIHSS score predicted from other measurements recorded at their baseline assessment. With exclusion of these patients, the numbers of IST-3 patients in each NIHSS categories would be 385, 972, 531, 559, and 344, respectively.

***Table 1*: Baseline characteristics of patients in participating trials**

Lancet Neurol. 2016 Aug;15(9):925-933.

Risk factors of post TPA bleeding

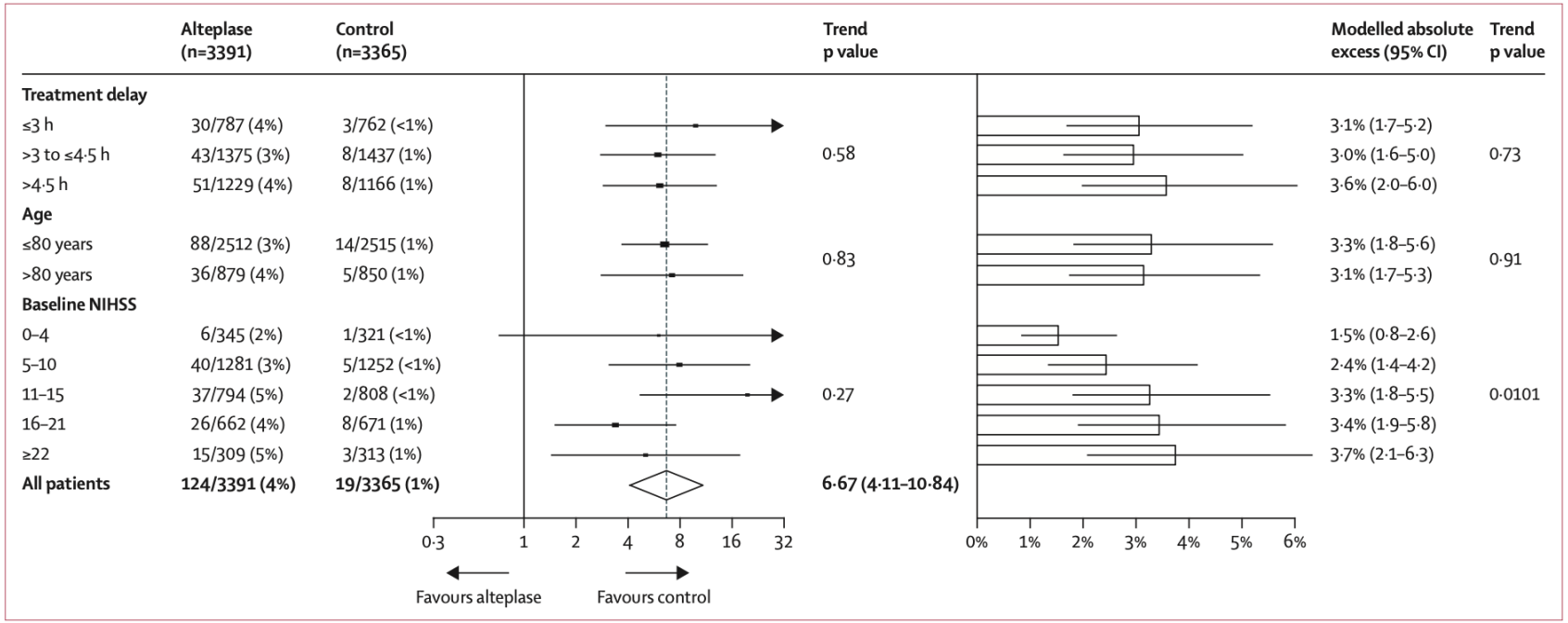


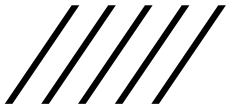
***Figure 2*: Effect of alteplase on SITS-MOST intracerebral haemorrhage at 24–36 h by time to treatment, age, and stroke severity**
For each of the three baseline characteristics shown, the OR subgroup estimates are derived from a single trial-stratified logistic regression model that allows for separate estimation of the OR in each of the subgroups after adjustment for the other two baseline characteristics (but not possible interactions with those characteristics). The overall effect (indicated by the open diamond) is the trial-stratified logistic regression estimate adjusted only for treatment allocation. The absolute excess risk (95% CI) for each subgroup is estimated by application of the OR seen among all randomly assigned patients (or its confidence limits) to the mean expected risk in control-allocated patients for that subgroup (estimated from a logistic regression model among all participants adjusted for trial, treatment allocation, the subgroup of interest, and mean levels of the other two baseline characteristics). SITS-MOST=Safe Implementation of Thrombolysis in Stroke Monitoring Study. OR=odds ratio. NIHSS=National Institutes of Health Stroke Scale.

- The proportional increase in the odds was similar irrespective of treatment delay, age, and stroke severity at baseline.
- While the underlying risk of intracerebral hemorrhage without alteplase increased with stroke severity.

Lancet Neurol. 2016 Aug;15(9):925-933.

Risk factors of post TPA bleeding

- For patients treated within 4.5 h, the absolute increase in the proportion (6·8% [4·0% to 9·5%]) achieving a modified Rankin Scale of 0 or 1 exceeded the absolute increase in risk of fatal intracerebral hemorrhage (2·2% [1·5% to 3·0%]) and the increased risk of any death within 90 days (0·9% [–1·4% to 3·2%]).



Lancet Neurol. 2016 Aug;15(9):925-933.

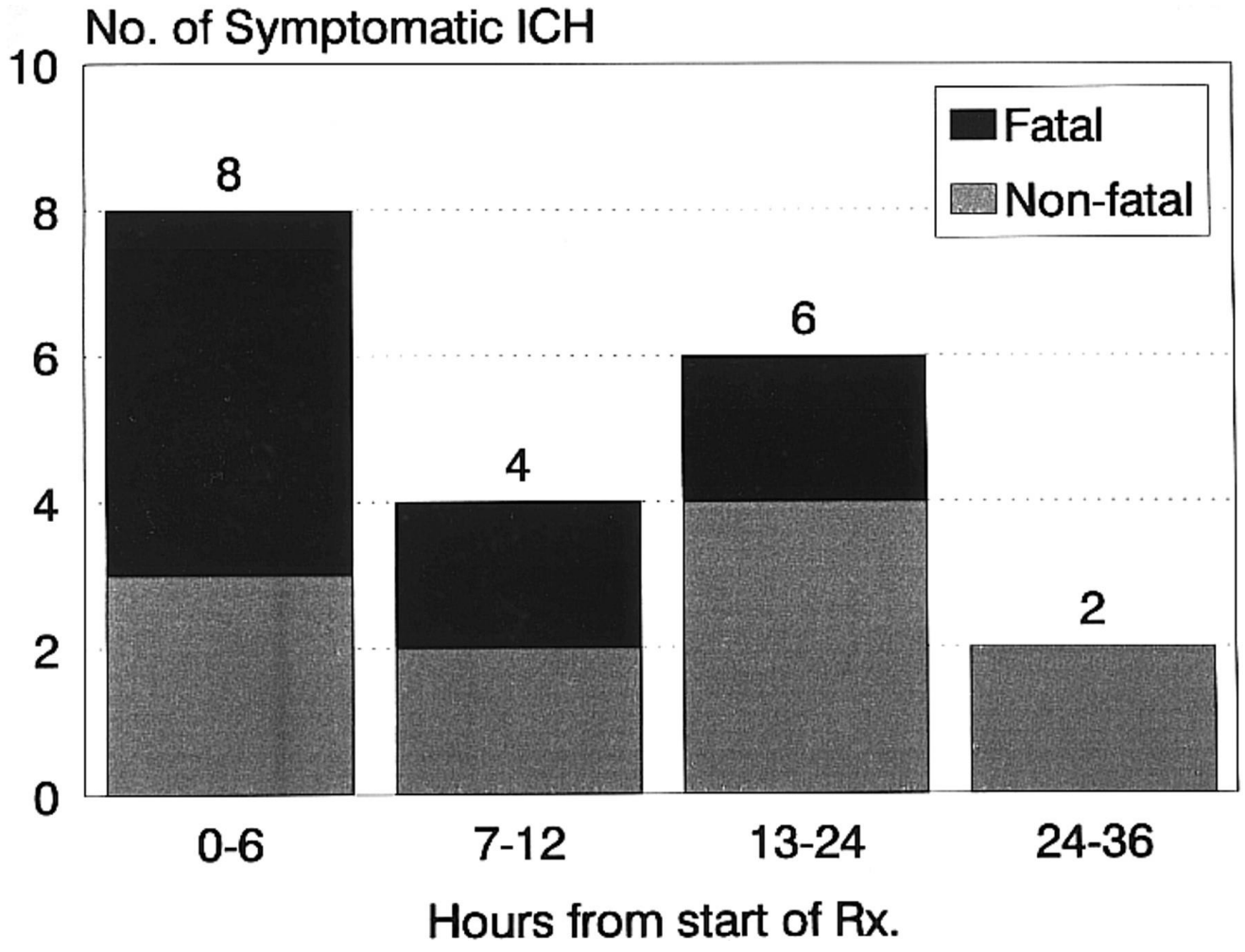
Timing of antiplatelet post TPA

2. The risk of antithrombotic therapy (other than IV aspirin) within the first 24 hours after treatment with IV alteplase (with or without mechanical thrombectomy) is uncertain. Use might be considered in the presence of concomitant conditions for which such treatment given in the absence of IV alteplase is known to provide substantial benefit or withholding such treatment is known to cause substantial risk.	IIb	B-NR	New recommendation.

Most SICH hemorrhages will occur within the first 24 hours after receiving IV r-tPA, with the bulk of fatal hemorrhages occurring within the first 12 hours.*

Stroke. 2019;50:e344–e418
*Stroke. 1997;28:2109–2118

Timing of antiplatelet post TPA



Stroke. 1997;28:2109–2118

Table 3. The distribution of ICH diagnosis time for patients with ICH 36 hours after thrombolysis

	sICH ($n=13$), %	asymptomatic ICH ($n=25$), %	P value
<12 hours ($n=13$)	9 (69.2%)	4 (30.8%)	0.003*
0-6 hours	6 (46.1%)	3 (23.1%)	
6-12 hours	3 (23.1%)	1 (7.7%)	
12-36 hours ($n=25$)	4 (16%)	21 (84%)	
12-18 hours	3 (12%)	2 (8%)	
18-24 hours	1 (4%)	10 (40%)	
24-36 hours	0	9 (36%)	

*$P<0.05$

J Atheroscler Thromb, 2020; 27: 1176-1182.

Risks and Benefits of Early Antithrombotic Therapy after Thrombolytic Treatment in Patients with Acute Stroke

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- Retrospective analysis of a single-center experience on the safety and efficacy of antithrombotic therapy (ATT) started before or after 24 h of intravenous thrombolysis in a cohort of acute ischemic stroke patients.
- A total of 139 patients (Rapid ATT group) received antithrombotic therapy before 24 h of thrombolysis, and 33 patients (Standard ATT group) after 24 h.
- At day 90, a greater proportion of patients in the rapid ATT group had shifted down the mRS, and had improved in the NIHSS score.

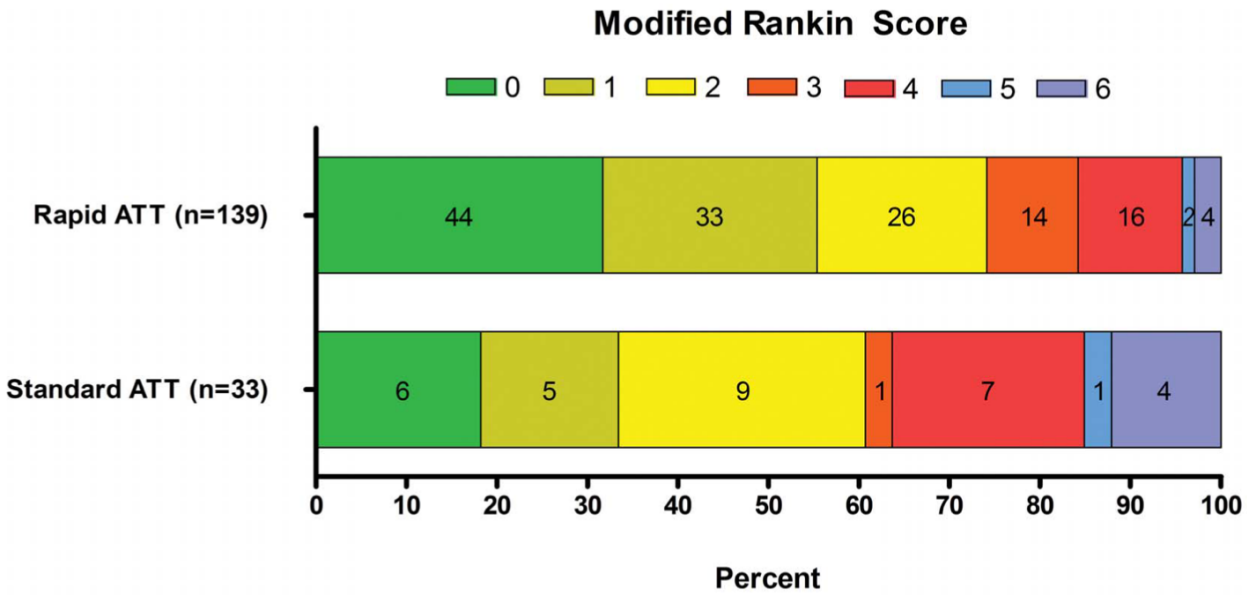
PLoS ONE 8(8): e71132.

Table 1. General characteristics of study population according to ATT onset group.

	Rapid ATT (n = 139)	Standard ATT (n = 33)	p
Age (years), median (IQR)	69 (60–76)	74 (63–78)	0.07
Males, n (%)	85 (61)	20 (61)	0.95
Pre-admission mRS, median (IQR)	0 (0–1)	0 (0–1)	0.82
Diabetes, n (%)	34 (25)	8 (24)	0.98
Smoking, n (%)	41 (30)	7 (21)	0.34
Hypertension, n (%)	92 (66)	25 (76)	0.29
Dyslipidemia, n (%)	60 (43)	12 (36)	0.48
Atrial Fibrillation, n (%)	29 (21)	9 (27)	0.43
Ischemic Heart Disease, n (%)	21 (15)	4 (12)	0.66
Peripheral Vascular Disease, n (%)	8 (6)	2 (6)	0.95
Previous stroke, n (%)	14 (10)	5 (15)	0.40
Previous antithrombotic use, n (%)	53 (38)	16 (49)	0.27
TOAST			0.81
Cardioembolism, n (%)	50 (36)	11 (33)	
Aterothrombotic, n (%)	28 (20)	5 (15)	
Lacunar, n (%)	16 (12)	4 (12)	
Undetermined, n (%)	33 (24)	11 (33)	
Other etiologies, n (%)	12 (8)	2 (6)	
Baseline Systolic BP (mmHg), median (IQR)	155 (140–170)	160 (131–170)	0.80
Baseline glucose (mg/dl), median (IQR)	124 (109–154)	119 (106–140)	0.54
Systemic rtPA plus endovascular tx, n (%)	28 (20)	5 (15)	0.51
Time to rtPA treatment (min), median (IQR)	123 (95–185)	130 (100–180)	0.80
ASPECT score at baseline CT, median (IQR)	10 (8–10)	10 (9–10)	0.40
Baseline NIHSS, median (IQR)	6 (3–14)	8 (4–12)	0.54
NIHSS at 24 h, median (IQR)	3 (1–8)	4 (0–15)	0.64
NIHSS at day 7, median (IQR)	2 (0–6)	3 (0–13)	0.24

Table 2. Vessel status at baseline and at 72 h in both att groups.

	Rapid ATT	Standard ATT	p
Vessel at end of Thrombolysis	N = 136	N = 33	**0,60**
Patent vessel, n (%)	74 (54)	20 (61)	
Proximal occlusion, n (%)	32 (24)	8 (24)	
Distal occlusion, n (%)	15 (11)	4 (12)	
Tandem occlusion, n (%)	15 (11)	1 (3)	
Vessel patency at day 3	N = 132	N = 28	**0,06**
TIMI 2–3, n (%)	126 (95)	25 (89)	
TIMI 0–1, n (%)	6 (5)	3 (11)	
Vessel re-occlusion at day 3	N = 71	N = 18	**0,20**
No, n (%)	71 (100)	17 (94)	
Yes, n (%)	0(0)	1 (6)	



PLoS ONE 8(8): e71132.

Stroke outcomes with use of antithrombotics within 24 hours after recanalization treatment

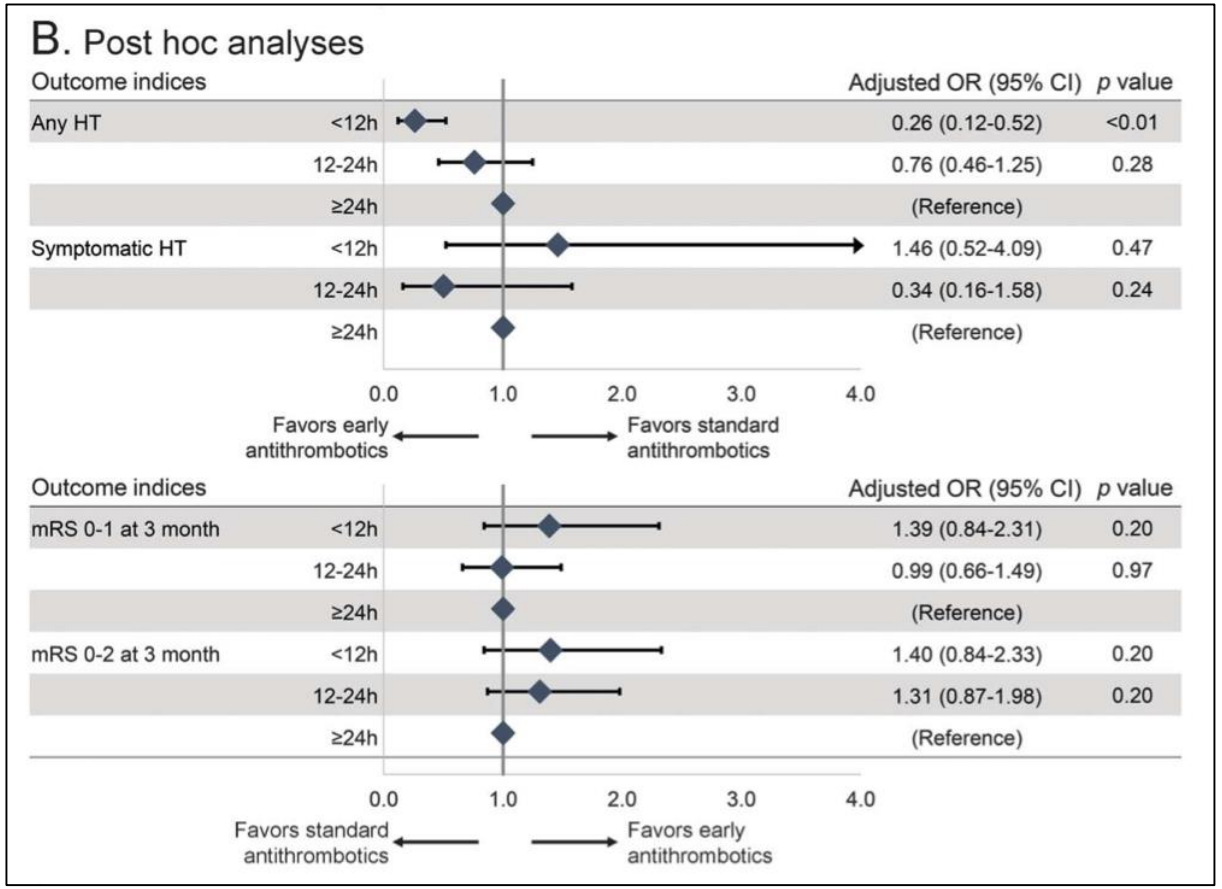
- A total of 712 patients who had an acute ischemic stroke and underwent IV or endovascular (intra-arterial [IA]) recanalization between July 2007 and March 2015 were selected.
- The recanalization treatment cases included in this study comprised 34% (n 243) IV only, 32% (n 229) IA only, and 34% (n 5 240) combined IV-IA strategies. Antithrombotics were administered within 24 hours in 64% (n 456) of the patients.
- Earlier initiation of antithrombotics was not associated with symptomatic hemorrhages (0.85; 0.35–2.10) or mRS scores of 0–1 at 3 months after stroke (1.09; 0.75– 1.59).
- The effects of earlier antithrombotics on the clinical outcomes were not significantly modified by the modality of recanalization treatment.

Neurology. 2016 Sep 6;87(10):996-1002.

Table 2 Utilization of antithrombotics after recanalization treatment

	All patients (n = 712)	Early antithrombotics (n = 456)	Standard antithrombotics (n = 256)
All patients			
Antiplatelet monotherapy	385 (54.1)	233 (51.1)	152 (59.4)
Antiplatelet dual therapy	219 (30.8)	162 (35.5)	57 (22.3)
Anticoagulant	99 (13.9)	54 (11.8)	45 (17.6)
Antiplatelet with anticoagulant	9 (1.3)	7 (1.5)	2 (0.8)
Time between recanalization treatment and antithrombotics, h	21.0 ± 14.2	13.9 ± 7.2	33.7 ± 14.7
Antiplatelet monotherapy	385	233	152
Aspirin	370 (96.1)	222 (95.3)	148 (97.4)
Clopidogrel	15 (3.9)	11 (4.7)	4 (2.6)
Antiplatelet dual therapy	219	162	57
Aspirin + clopidogrel	215 (98.2)	160 (98.8)	55 (96.5)
Aspirin + cilostazol	4 (1.8)	2 (1.2)	2 (3.5)
Anticoagulant	99	54	45
LMWH	15 (15.2)	8 (14.8)	7 (15.6)
UFH	40 (40.4)	24 (44.4)	16 (35.6)
Dabigatran	25 (25.3)	12 (22.2)	13 (28.9)
Rivaroxaban	4 (4.0)	2 (3.7)	2 (4.4)
Warfarin	15 (15.2)	8 (14.8)	7 (15.6)
Antiplatelet with anticoagulant	9	7	2
Aspirin + LMWH	2 (22.2)	1 (14.3)	1 (50.0)
Aspirin + UFH	4 (44.4)	4 (57.1)	0 (0.0)
Aspirin + dabigatran	1 (11.1)	0 (0.0)	1 (50.0)
Aspirin + clopidogrel + UFH	2 (22.2)	2 (28.6)	0 (0.0)

Abbreviations: LMWH = low-molecular-weight heparin; UFH = unfractionated heparin. Values are n (%).



Neurology. 2016 Sep 6;87(10):996-1002.

The safety and effectiveness of early anti-platelet therapy after alteplase for acute ischemic stroke: A meta-analysis

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- The 3 studies included a total of 1008 participants, of which 600 (59.5%) participants were randomly assigned to use of anti-platelet aggregation drugs within 24 h and 408 (40.5%) were assigned to the control group.
- The results showed that the early treatment group did not affect the 90-day efficacy (relative risk 1.13; 95% Confidence interval (0.97 – 1.32; P = 0.12). But there was significant heterogeneity between studies
- In terms of safety assessment, the early use of anti-platelet aggregation drugs after thrombolysis had a neutral effect on the risk of symptomatic cerebral hemorrhage, asymptomatic cerebral hemorrhage, and bleeding from other systemic sites.

J Clin Neurosci. 2021 Sep;91:176-182.

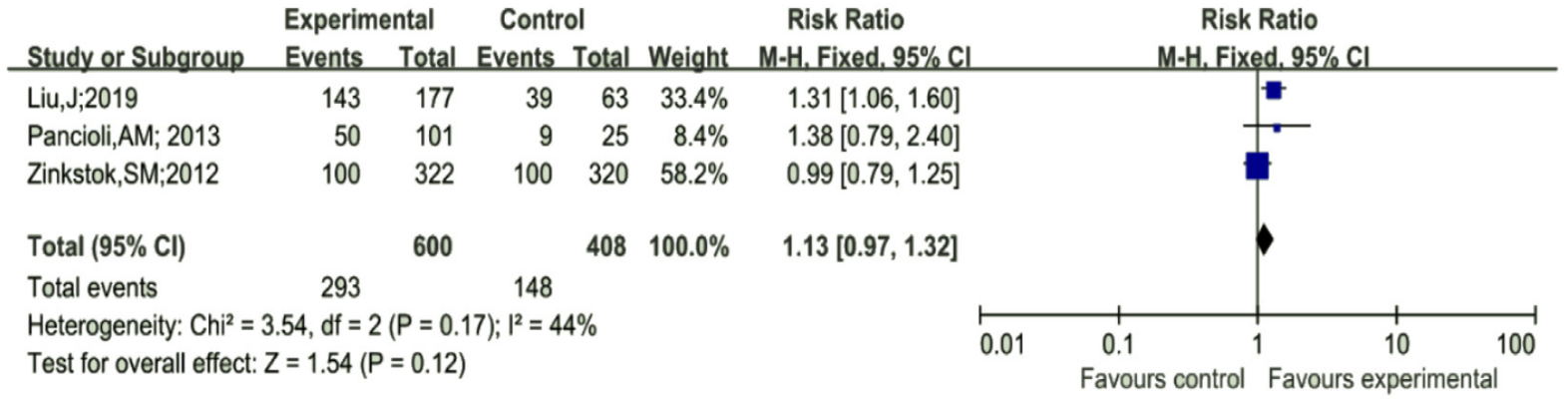

Fig. 2. 90-day efficacy evaluation (mRS score 0–1 ratio) (early anti-platelet-aggregation treatment compared with control group).

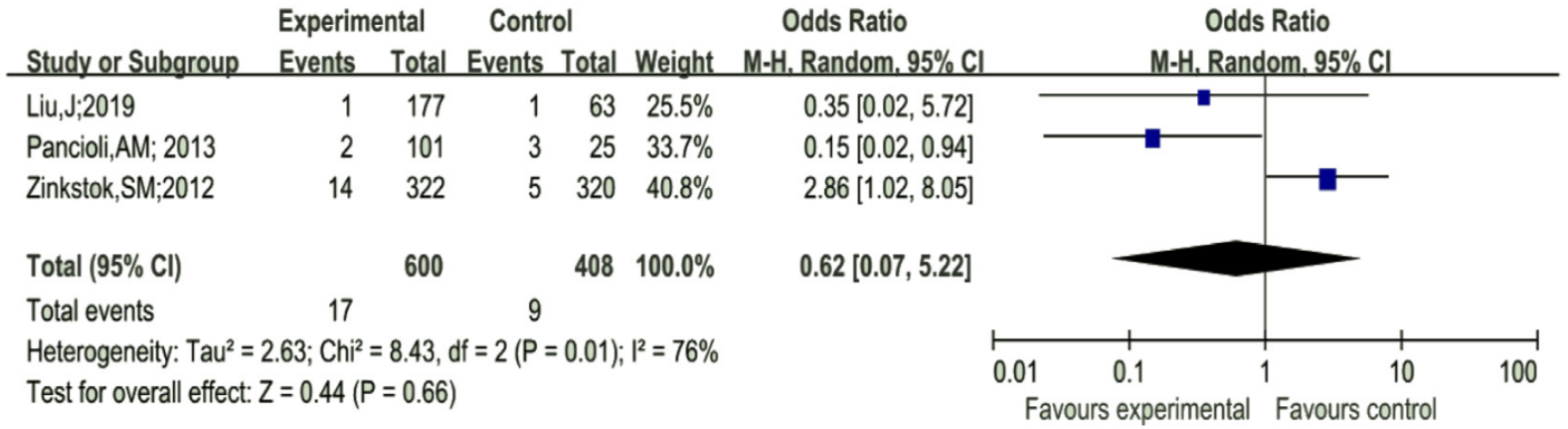

Fig. 3. Incidence of intracranial hemorrhage (compared to control group for early anti-platelet-aggregation treatment).

Antiplatelet therapy within 24 hours of tPA: lessons learned from patients requiring combined thrombectomy and stenting for acute ischemic stroke

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- A retrospective studied the safety of early (< 24 hrs) post-tPA antiplatelet use by reviewing patients who underwent MT and stent placement for acute ischemic stroke.
- Six patients were included, median NIHSS was 14.
- Median time from symptom onset to IV tPA was 120 min (IQR 78-204 min). Median time between tPA and anti-platelet administration was 4.9 hours (IQR 3.0-6.7 hours).
- Clots were successfully removed from ICA or MCA in 5 patients, the vertebrobasilar junction in one patient.
- The median time from stroke onset to endovascular access was 185 min (IQR 136-417 min). No patients experienced symptomatic post-procedure intracranial hemorrhage (ICH). Median modified Rankin Scale score on discharge was 3.5.

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Table 1. Patient characteristics and outcomes

No.	Age	Sex	Initial NIHSS	Pre-op NIHSS	Etiology	tPA	Angio plasty	Stent Site	MT Site	OTT	OMT	TAT	TICI	HT	Discharge mRS	30d mRS	90d mRS
1	64	M	15	〃	Stenosis	IV	Yes	R ICA	R ICA terminus, L A1/A2	0:57	2:19	10:49*	2B	0	4	NA	4
2	30	M	21	〃	Dissec-tion	IA	No	L ICA	L ICA terminus	3:35	0:49	1:53	2B	0	3	2	2
3	54	M	18	〃	Dissec-tion	IV	No	L ICA	L M1	1:18	2:15	3:01	2B	0	3	NA	NA
4	53	M	13	〃	Stenosis	IV	No	R ICA	R M2	2:28	3:52	3:10	2B	0	2	2	NA
5	56	M	1	17	Dissec-tion	IV	No	L CCA	L M2	2:00	7:59	6:41	2B	0	5	NA	NA
6	70	M	3	14	Stenosis	IV	Yes	BA	L VB junction	3:24	12:27	10:53	2B	0	6	6	6

* Antiplatelet administration delayed by contrast extravasation versus hemorrhage on post-operative head CT.
NIHSS, National Institutes of Health Stroke Scale; tPA, tissue plasminogen activator [route of administration]; IV, intravenous; IA, intraarterial; MT, mechanical thrombectomy; ICA, internal carotid artery; CCA, common carotid artery; BA, basilar artery; VB, vertebrobasilar; OTT, Onset-to-tPA time (hour:minute); OMT, Onset-to-thrombectomy time (hour:minute); TAT, tPA-to-antiplatelet therapy time (hour:minute); TICI, thrombolysis in cerebral infarction; HT, hemorrhagic transformation; mRS, Modified Rankin Scale

Take home message

- For patients treated with tPA within 4.5 h, the absolute increase in achieving a mRS of 0 or 1 (6.8%) exceeded the absolute increase in risk of fatal ICH (2·2%) and any death within 90 days (0·9%).
- Risk factors of sICH post tPA are varies between studies; severity of stroke, prior stroke, atrial fibrillation, antiplatelet use, ASPECT ≤7.
- Most SICH hemorrhages will occur within the first 24 hours after receiving IV r-tPA, with the bulk of fatal hemorrhages occurring within the first 12 hours.
- Recent studies showed no significant different of sICH between early antiplatelet use within 24 hours and standard treatment.
- In one study demonstrated at day 90, a greater proportion of patients in early antithrombotic therapy group had shifted down the mRS, and had improved in the NIHSS score more than control group.

THANK YOU