THE CURRENT ROLE OF HEMOSTATIC AGENTS IN THE MANAGEMENT OF SPONTANEOUS INTRACEREBRAL HEMORRHAGE

A presentation for HealthTrust Members
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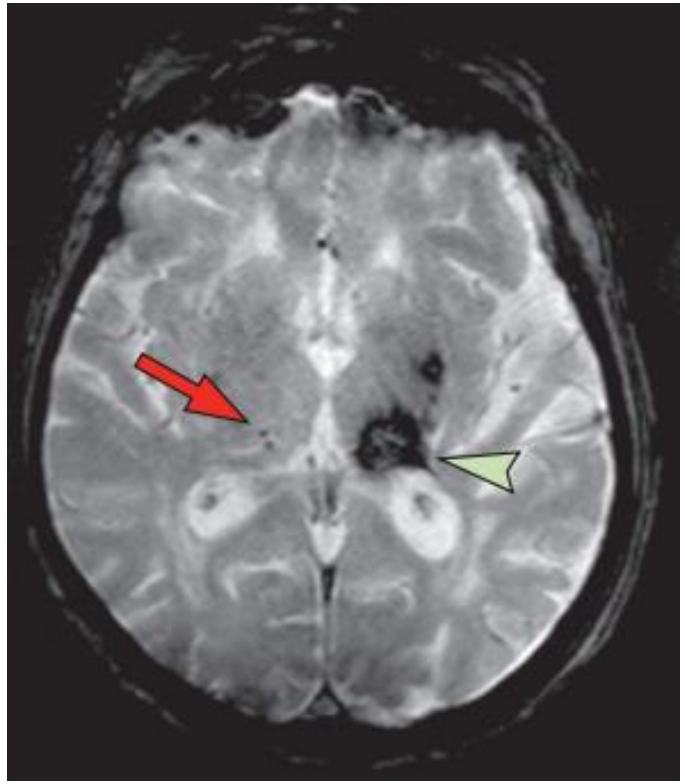
OBJECTIVES

Identify common clinical presentations, risk factors, and pathophysiology of spontaneous intracerebral hemorrhages

Recall current guideline recommendations on acute management of spontaneous intracerebral hemorrhages

Recognize the optimal time to administer hemostatic agents in specific subgroups of patients presenting with spontaneous intracerebral hemorrhage

SPONTANEOUS INTRACEREBRAL HEMORRHAGE (SICH)



Red arrow: Microhemorrhage
Green arrow: deep hematoma

Defined as a brain injury attributable to a non-traumatic formation of a hematoma in the brain parenchyma

Accounts for 10-15% of all strokes worldwide and is the most common type of intracranial hemorrhage[1,2,3]

Affects ~2 million people per year[1]

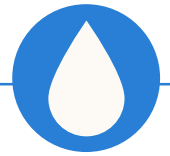
1 out of 3 patients die within the first month of onset and only 20% regain functional independence[1,2,3]

Sources: Lancet 2018; 392: 1257–68.
Stroke. 2022;53:e282–e361.
N Engl J Med. 2022 Oct; 387:1589-1596.
N Engl J Med. 2005 Feb 24;352(8):777-85.

RISK FACTORS

HYPERTENSION

Strongest risk factor for SICH



ANTICOAGULATION

~15% of SICH[1]

Both warfarin and NOACs associated with worse outcomes

CEREBRAL AMYLOID ANGIOPATHY

Associated with high risk of rebleeding (~9%/year)[2]

OLDER AGE

Associated with higher rates of amyloid deposition and worse prognosis

RACE

2 times as high in Asian populations[3]

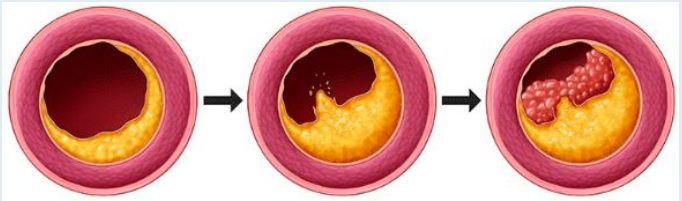
1.6 times as high in black and Hispanic populations[3]

NOAC: Novel Oral Anti-Coagulant

Source: Schizodimos T, et al. J Anesth. 2020 Oct;34(5):741-757.
Stroke. 2022;53:e282–e361.
Lancet 2018; 392: 1257–68
N Engl J Med. 2022 Oct; 387:1589-1596.

VASCULAR CAUSES

Arteriolosclerosis



Hyalinized vascular wall thickening

Occurs in deeper areas of brain (Thalamus, brain stem, basal ganglia)

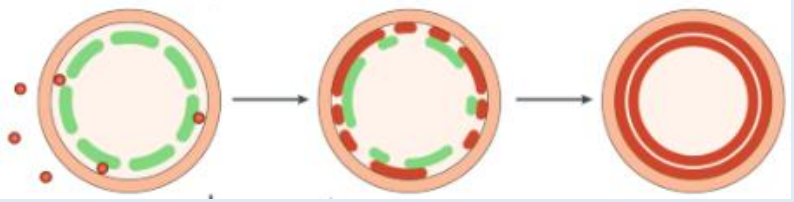
Age, hypertension, and diabetes

Small subset develop SICH

"ICH-prone" environment

Also, risk factors for ischemic stroke

Cerebral Amyloid Angiopathy



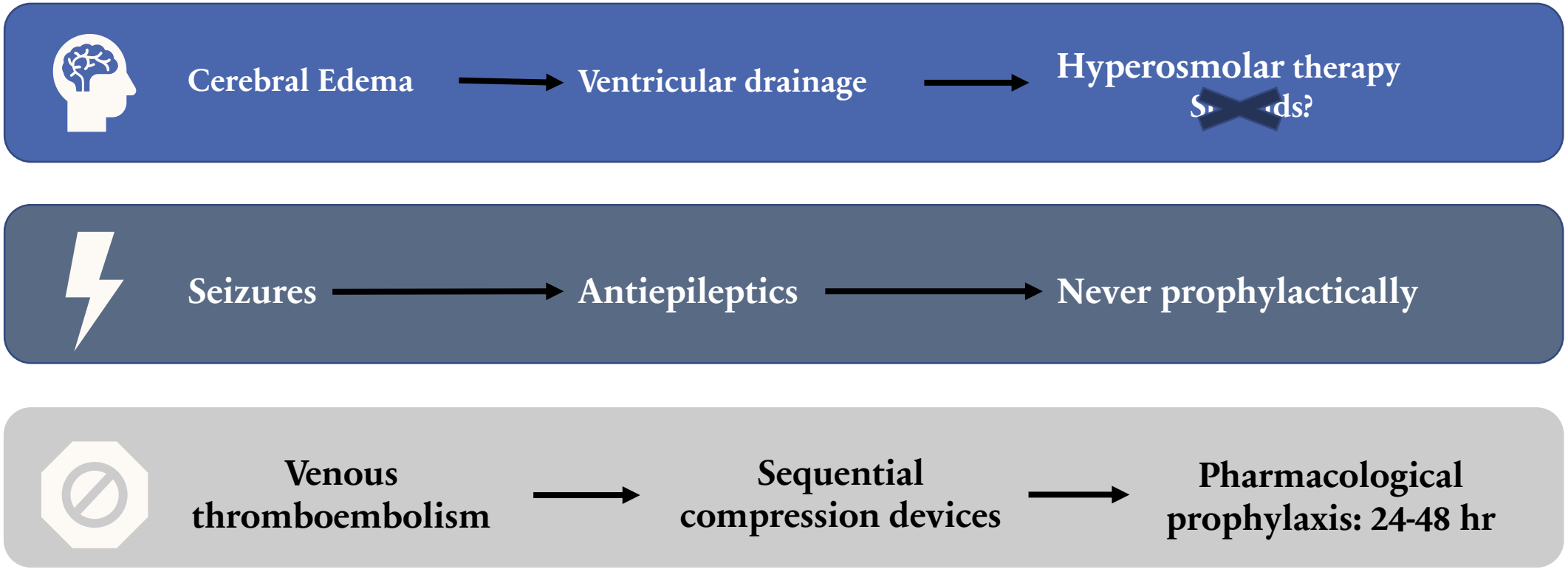
Deposition of β-amyloid peptide

Occurs in cerebral cortex and lobar regions

Age and apolipoprotein E genotypes

Source: Stroke. 2022;53:e282–e361.

COMPLICATIONS OF SICH



Source: Stroke. 2022;53:e282–e361.

MEDICAL MANAGEMENT

There is currently no medical therapy that has demonstrated a clear benefit in patients presenting with a SICH

Hematoma Expansion is a poor prognostic marker associated with increased mortality and disability in patients presenting with ICH

Therefore, most of our medical therapies target hematoma expansion to potentially to improve clinical outcomes

- Acute Blood Pressure Management
- Hemostasis
- Surgery

Source: Stroke. 2022;53:e282–e361.

BLOOD PRESSURE MANAGEMENT

ATACH-2

- Patients with ICH to 1 of 2 BP goals:
  1. SBP: 110-139 mmHg
  2. SBP: 140 to 180 mmHg
- No difference in clinical outcomes
- Increased renal adverse events with more intensive group

BLOOD PRESSURE GOALS (AHA)

1. BP range of 130-150 mmHg within 2 hr of onset and within 1 hr of treatment (2b)
2. Titration to ensure smooth, sustained control of BP (2a)
3. Avoid SBP < 130 mmHg (3)

Based largely off two trials

INTERACT-2

- Patients with ICH to 1 of 2 BP goals:
  1. SBP <140 mmHg
  2. SBP <180 mmHg
- Improved functional outcomes
- No difference in renal adverse events

Post-Hoc analysis of INTERACT-2 showed increased standard deviation of SBP within 24 hr associated with increased disability and death

Sources: Lancet 2018; 392: 1257–68
Stroke. 2022;53:e282–e361.
N Engl J Med. 2022 Oct; 387:1589-1596.

HEMOSTASIS

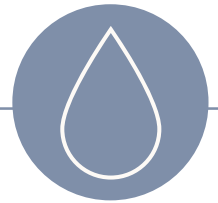
WARFARIN

IV Vitamin K
+
4-Factor Prothrombin Complex Concentrate (4F-PCC)

NOACS

Xa Inhibitors
Andexanet alfa (preferred)
or
4F-PCC

Dabigatran
Idarucizumab (preferred)



HEPARINS

Protamine

Antiplatelet

Guidelines state to avoid platelet transfusions | RCT of 190 patients showed worse outcomes

Sources: Lancet 2018; 392: 1257–68
Stroke. 2022;53:e282–e361.
N Engl J Med. 2022 Oct; 387:1589-1596.

ASSESSMENT QUESTION 1

Which of the following is not a risk factor for a spontaneous intracerebral hemorrhage?

a. Hypertension
b. Anticoagulation
c. Caucasian race
d. Older age

ASSESSMENT QUESTION 1 CORRECT RESPONSE

Which of the following is not a risk factor for a spontaneous intracerebral hemorrhage?

a. Hypertension
b. Anticoagulation
c. Caucasian race
d. Older age

ASSESSMENT QUESTION 2

A 67 year old male with a past medical history of hypertension, dyslipidemia, and type 2 diabetes mellitus presents with left sided weakness, slurred speech, and left facial droop. Last known well was 3 hours prior to admit. CT of head reveals an intracranial hemorrhage. Patient's blood pressure is 168/72 mmHg. Which of the following strategies is the BEST for acute blood pressure reduction?

a. Clevidipine titrated to achieved BP between 130 to 150 mmHg within 1 hour of initiation
b. Cardene titrated to achieve BP target of <140 mmHg within 2 hours of treatment initiation
c. IV hydralazine titrated to achieve BP between 130 to 150 mmHg within 1 hour of initiation
d. Clevidipine titrated to achieve BP target of <140 mmHg within 2 hours of treatment initiation

ASSESSMENT QUESTION 2 CORRECT RESPONSE

A 67 year old male with a past medical history of hypertension, dyslipidemia, and type 2 diabetes mellitus presents with left sided weakness, slurred speech, and left facial droop. Last known well was 3 hours prior to admit. CT of head reveals an intracranial hemorrhage. Patient's blood pressure is 168/72 mmHg. Which of the following strategies is the BEST for acute blood pressure reduction?

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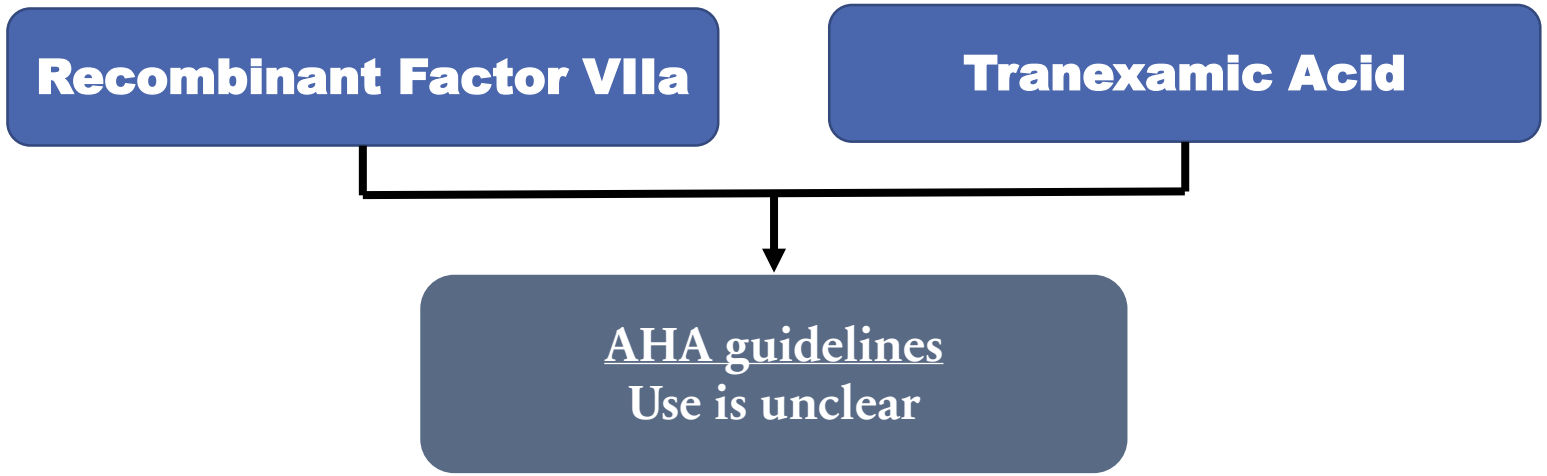
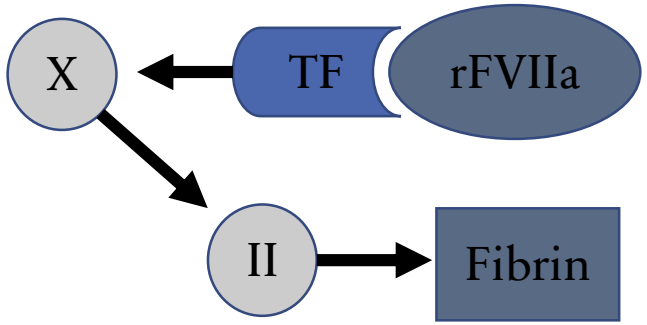
GENERAL HEMOSTASIS



Source: Stroke. 2022;53:e282–e361.

RECOMBINANT FACTOR VIIA (RFVIIA)



Mechanism of Action

rFVIIa binds to tissue factor (TF) at sites of tissue injury/vascular wall disruption → Activation of factor X → Fibrin deposition → Coagulation → Hemostasis

Rationale for Use in SICH

Hemophiliacs and Perioperative Use

Induce coagulation in patients with hemophilia who have reduced VIII or IX activity

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Reduces perioperative bleeding in patients undergoing surgery

Source: N Engl J Med. 2005 Feb 24;352(8):777-85

Factor VIIa Phase 2b Trial

Study Design	Double-blind, randomized, placebo-controlled trial across 20 countries in 73 hospitals
Objective	"…to determine whether rFVIIa can effectively reduce hematoma growth in patients with acute intracerebral hemorrhage, and thus improve their outcomes"

Inclusion

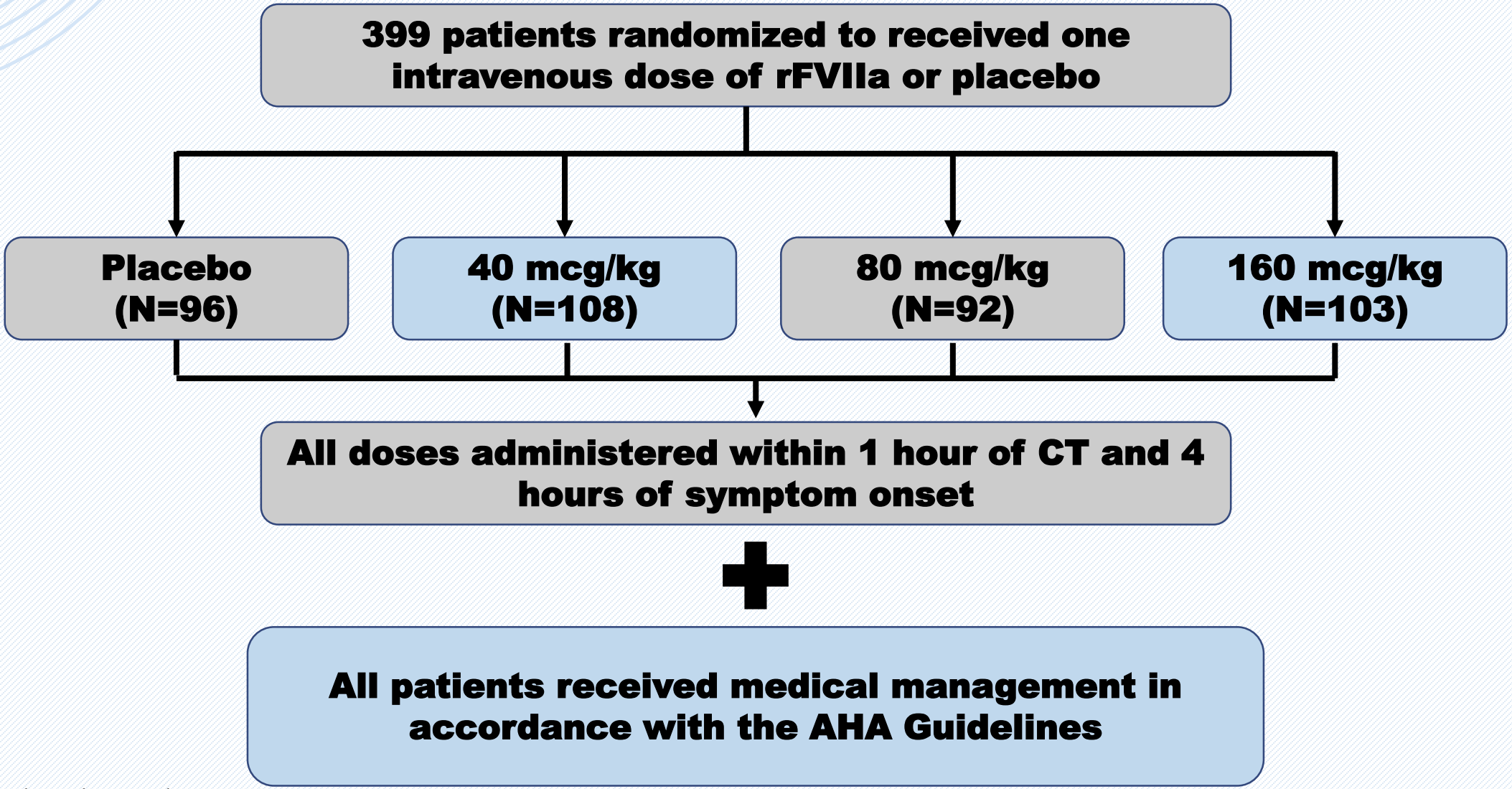
- ≥18 years of age
- CT scan of primary, spontaneous intracerebral hemorrhage
- Symptom onset within 3 hours
- Glasgow Coma Scale (GCS) >5

Exclusion

- Planned surgical intervention within 24 hr
- modified Rankin Scale (mRS) >2 prior to ICH
- Oral anticoagulant use
- Any coagulopathy
- Any symptomatic thrombotic or vaso-occlusive disease within 30 days

Source: N Engl J Med. 2005 Feb 24;352(8):777-85

Intervention



Source: N Engl J Med. 2005 Feb 24;352(8):777-85

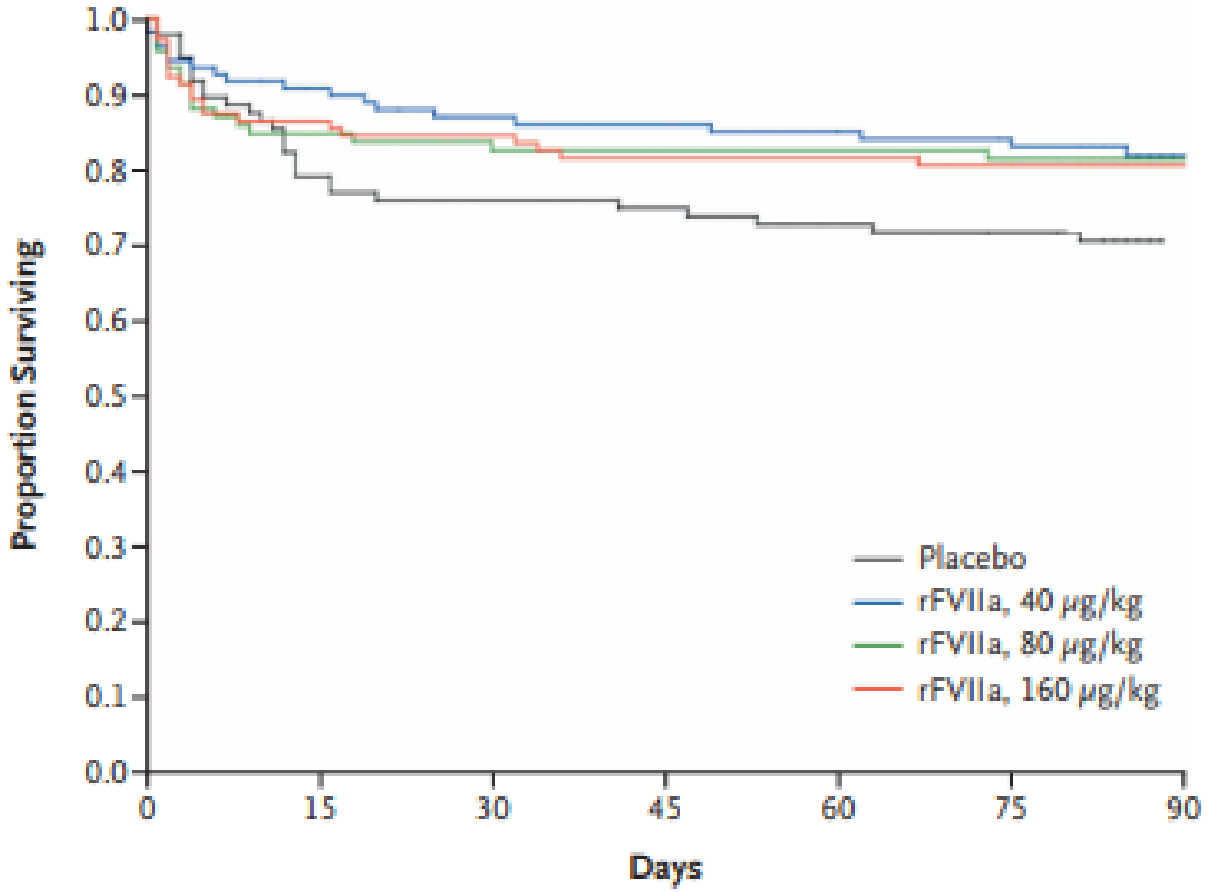
Baseline Characteristics

Variable	Placebo (N=96)	40 mcg/kg (N=108)	80 mcg/kg (N=92)	160 mcg/kg (N=103)
Age (yr)	68	67	65	64
Male (%)	53	63	61	67
White (%)	81	77	86	80
NIHSS	15	14	12	14
GCS	14	14	15	14
Mean time from onset to treatment (min)	165	173	167	165
Treated <3 hr after onset (%)	72	62	76	71

Source: N Engl J Med. 2005 Feb 24;352(8):777-85

Efficacy Outcomes

Hematoma Expa (% Increas	
Dose	% (98.3%
Placebo	29 (16 to
40 mcg/kg	16 (4 to
80 mcg/kg	14 (2 to
160 mcg/kg	11 (0 to
Combined	14 (7 to



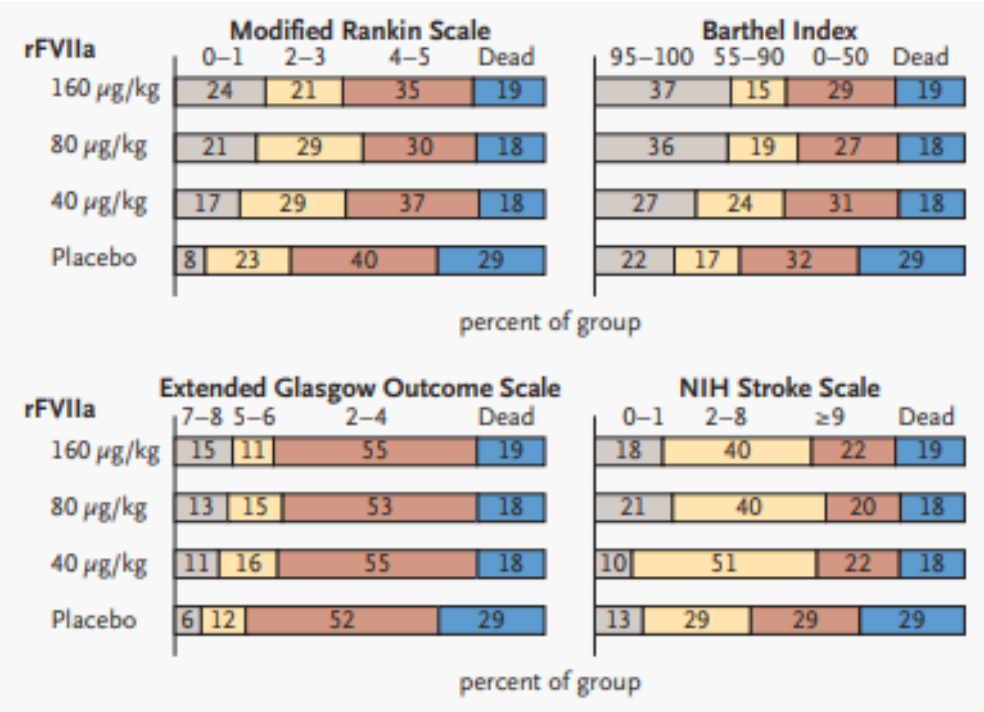
l at 90 Days		
	OR (95% CI)	P-Value
	-	-
	1.9 (1.0 to 3.8)	0.05
	1.8 (0.9 to 3.6)	0.10
	1.7 (0.9 to 3.3)	0.11
	1.8 (1.1 to 3.0)	0.02

More pronounced effec
treated within 3 hours of symptom onset
(P=0.009)

Source: N Engl J Med. 2005 Feb 24;352(8):777-85

Efficacy & Safety Outcomes

Unfavorable Outcomes Based on Various Scales								
	MRS		E-GCS		NIHSS		Barthel Index	
Dose	OR (95% CI)	P-Value	OR (95% CI)	P-Value	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Combined	1.8 (1.1 - 3.0)	0.004	1.4 (0.7 - 3.0)	0.14	-	0.008	-	0.006



Thromboembolic (TE) Events	
Dose	No. (%)
Placebo	2 (2)
40 mcg/kg	7 (6)
80 mcg/kg	4 (4)
160 mcg/kg	10 (10)
Combined	21 (7)

No difference in mortality or functional outcomes due to TE

Source: N Engl J Med. 2005 Feb 24;352(8):777-85

Conclusion

Strengths

- Analyzed multiple doses
- Analyzed timing of treatment
- Combined unfavorable outcomes
- Placebo group had similar rates of HE when compared to other studies

Weaknesses

- Placebo group was noted to have lower mortality than expected when compared to other population studies
- Underpowered subgroup of patients treated within time of 3-4 hours

Conclusion

- Ultra-early hemostatic therapy (within 4 hr of onset) with rFVIIa limits the growth of hemorrhage, reduces mortality, and improves functional outcomes after intracerebral hemorrhage
- rFVIIa should be administered with caution to patients with ICH who have risk factors for thromboembolic disease

Source: N Engl J Med. 2005 Feb 24;352(8):777-85

FAST Trial

Study Design	Multi-center, double-blind, randomized, placebo-controlled trial across 22 countries at 122 hospitals
Objective	To evaluate the effects of 20 mcg/kg and 80 mcg/kg of rFVIIa on rates of death and severe disability after intracerebral hemorrhage

Inclusion

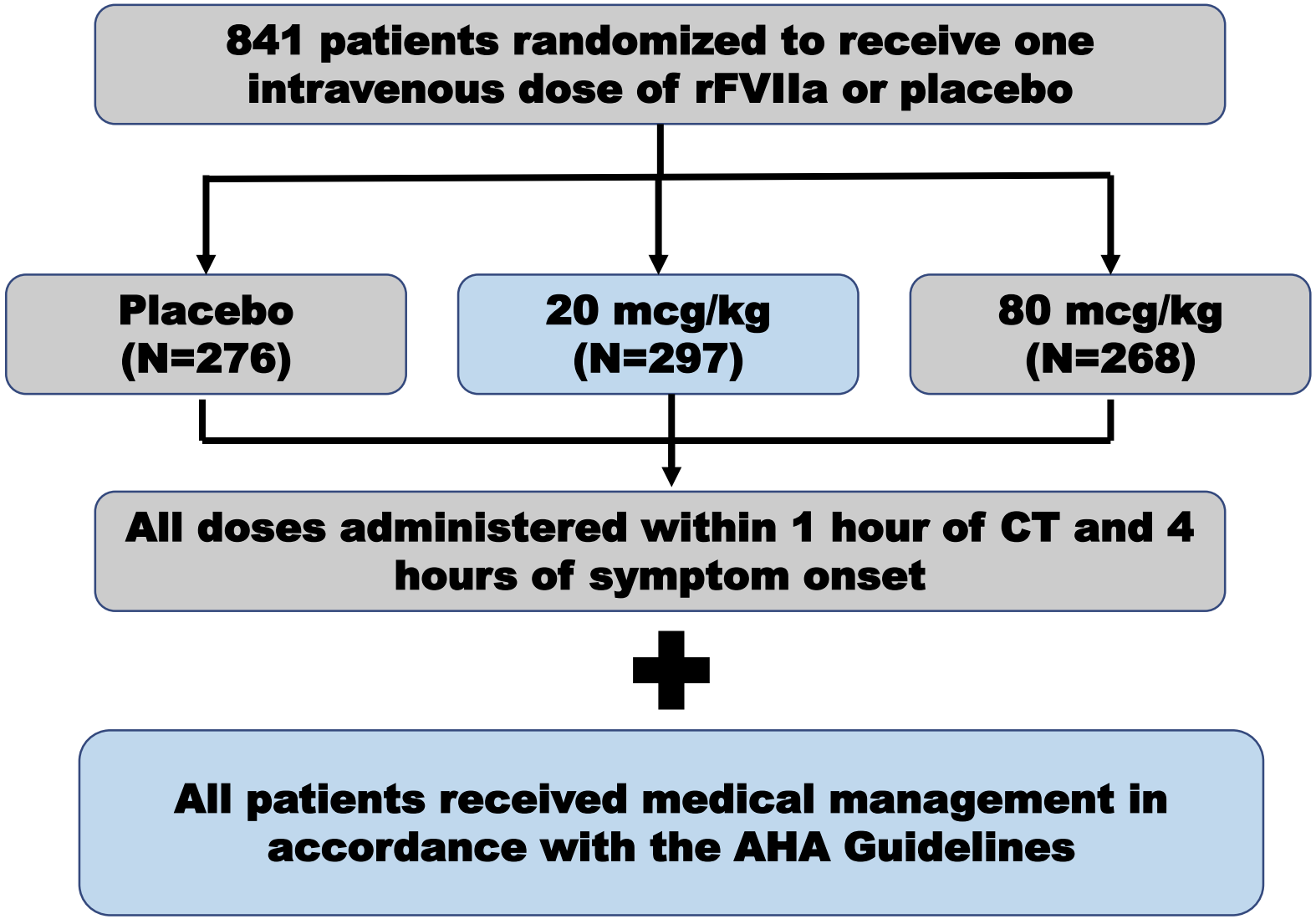
- ≥18 years of age
- CT scan of spontaneous intracerebral hemorrhage
- Symptom onset within 3 hours
- GCS >5

Exclusion

- Planned surgical intervention within 24 hr
- mRS >2 prior to ICH
- Oral anticoagulant use
- Any coagulopathy potential
- Any symptomatic thrombotic or vaso-occlusive disease within 30 days

Source: N Engl J Med. 2005 Feb 24;352(8):777-85

Intervention



Source: N Engl J Med. 2008 May 15;358(20):2127-37

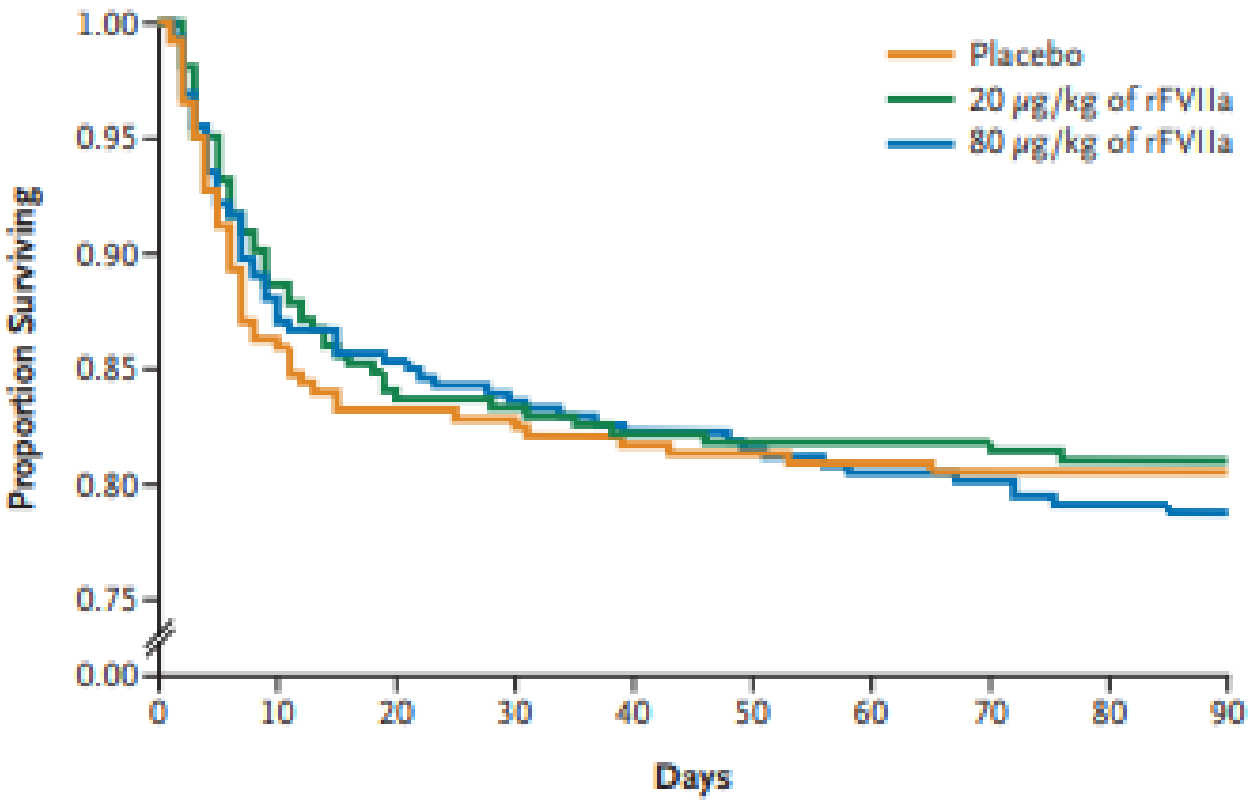
Baseline Characteristics

Variable	Placebo (N=268)	20 mcg/kg (N=276)	80 mcg/kg (N=297)
Age (yr)	65	65	65
Male (%)	63	61	61
White (%)	67	72	69
NIHSS	13	13	13
GCS	15	14	14
Intraventricular hemorrhage (%)	29	35	41
Baseline volume (mL)	22	24	23
Time from onset to treatment (min)	160	161	160
Treated <3 hr after onset (%)	72	72	74
Treated <2 hr after onset (%)	17	17	17

Source: N Engl J Med. 2008 May 15;358(20):2127-37

Efficacy Outcomes

Hematom (% I	
Dose	%
Placebo	26
20 mcg/kg	18
80 mcg/kg	11



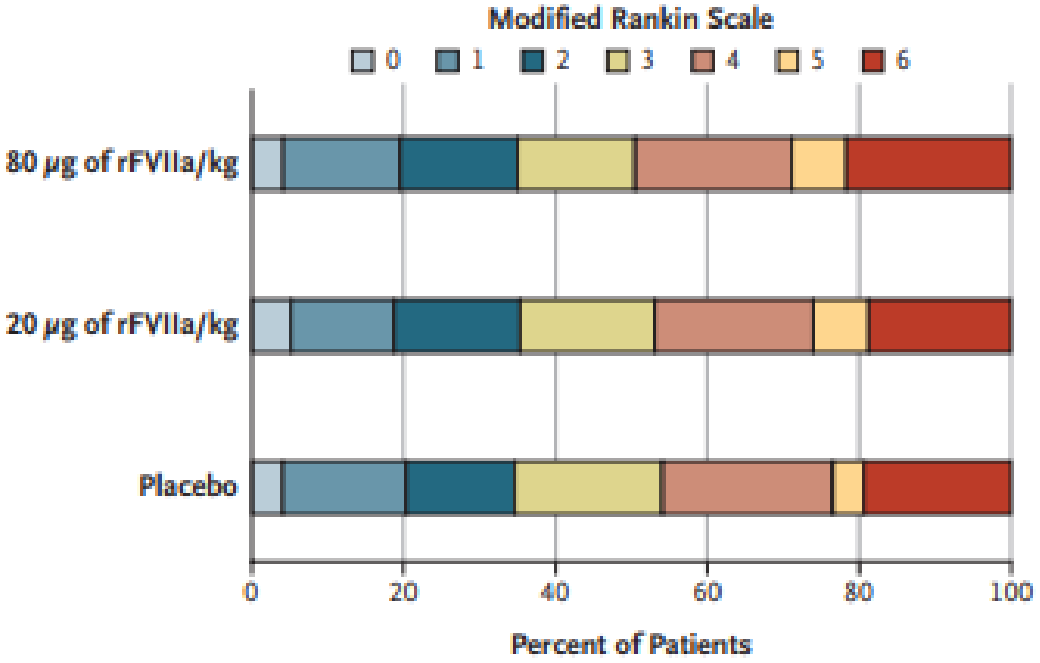
t Day 90	
OR (95% CI)	P-Value
-	-
0.8 (0.5 to 1.4)	0.38
.1 (0.7 to 31.8)	0.75

More pronounced
patients treated within 2 and 3 hours of
symptom onset

Source: N Engl J Med. 2008 May 15;358(20):2127-37

Efficacy & Safety Outcomes

Unfavorable Outcomes Based on Various Scales						
	MRS		NIHSS		Barthel Index	
Dose	OR (95% CI)	P-Value	Median	P-Value	Median	P-Value
20 mcg/kg	1.0 (0.6 – 1.6)	-	5	0.2	72.5	0.54
80 mcg/kg	1.4 (0.9 to 2.2)	-	4	0.02	70.0	0.91



TE Events	
Dose	No. (%)
Placebo	21 (8)
20 mcg/kg	24 (9)
80 mcg/kg	31 (10)

Higher rates in 80 mcg/kg group on arterial TE events (P = 0.04)

Source: N Engl J Med. 2008 May 15;358(20):2127-37

Conclusion

Strengths

- Looked at multiple doses to analyze dose dependent effects
- Analyzed timing of treatment for effect on HE volume increase
- Combined unfavorable outcomes into outcome

Weaknesses

- Randomization imbalances (Intraventricular hemorrhage)
- Placebo group was noted to have significantly worse poor functional outcome and mortality than expected when compared to prior phase 2b trial

Author's Conclusion

- rFVIIa reduced hematoma growth
- Reduced hematoma growth did not translate into a reduced rate of death or severe disability after intracerebral hemorrhage.

Source: Stroke. 2009 Mar;40(3):833-40.

POST-HOC ANALYSIS

Rationale	Results from FAST differed significantly from Phase 2b trial Earlier treatment and 80 mcg/kg rFVIIa associated with improved outcomes Patients with known risk for poor outcome at baseline may confound results of hemostatic agents on positive outcomes
Design	Performed univariate assessments on various factors and their effect on the odds of poor outcome to identify which patients to include for their subgroup analysis

Source: Stroke. 2009 Mar;40(3):833-40.

SUBGROUP AND RESULTS

Predictors of Better Outcomes

Treatment time <150 minutes — Age <70	Baseline hematoma volume <60 mL — Baseline IVH volume <5 mL

Variable	Placebo (N=59)	80 mcg/kg (N=55)
Age (yr)	56	56
NIHSS	14	13
GCS	14	14
Intraventricular hemorrhage (%)	20	20
Time from onset to treatment (min)	122	123

Source: Stroke. 2009 Mar;40(3):833-40.

Outcomes

Outcome	Placebo (N=59)	80 mcg/kg (N=55)	OR (95% CI)	P-Value
90-day mortality No. (%)	6 (10)	3 (5)	0.4 (0.1 to 1.8)	0.21
mRS (Unfavorable outcomes) No. (%)	11 (19)	5 (9)	0.28 (0.08 to 1.06)	0.03
HE (Mean % Increase)	39.2	13.9	-	0.01
Serious TE No. (%)	6 (10)	9 (16)	-	-

Author's Conclusion

- Early administration of rFVIIa does not result in consistent clinical benefit without considering other factors
- Further studies are warranted to explore the potential benefits of rFVIIa in specific patients presenting with spontaneous ICH

Source: Stroke. 2009 Mar;40(3):833-40.

SPOTLIGHT AND STOP-IT Trials

Study Design

Pooled analysis of 2 phase-II trials (SPOTLIGHT and STOP-IT)

Both were multi-center, double-blinded, placebo-controlled, randomized trials

Objective

To investigate whether recombinant activated coagulation factor VII (rFVIIa) reduces hemorrhage expansion among patients with spot sign–positive ICH

Inclusion

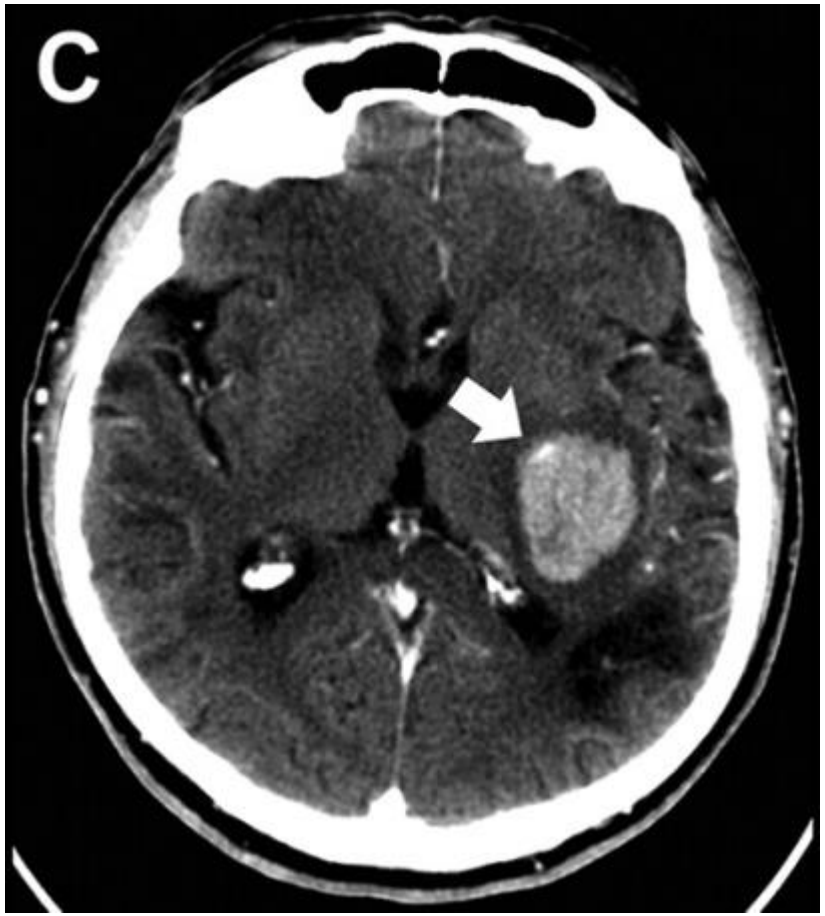
- ≥18 years of age
- CT scan of primary, spontaneous intracerebral hemorrhage with positive spot sign
- Treatment within 6 to 6.5 hours of onset of symptoms

Exclusion

- Planned surgical intervention
- Oral anticoagulant use
- Cardiac or cerebral ischemia, elevated risk of myocardial infection, or thromboembolism

Source: Stroke. 2009 Mar;40(3):833-40.

CT Spot Sign



White Arrow: CT Spot Sign

Prognostic and Treatment Implications

Represents extravasation of contrast material within the hematoma

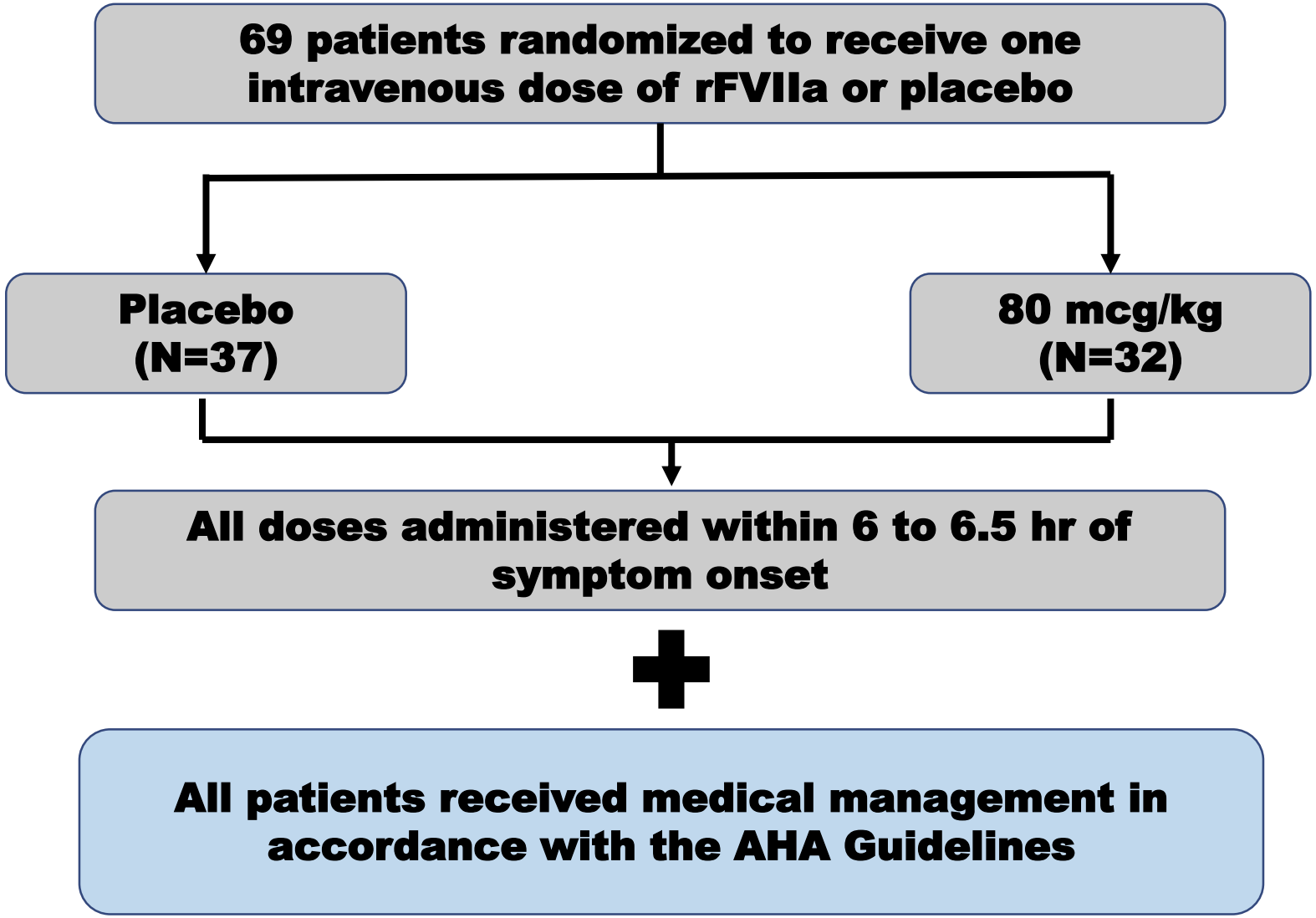
Indicator of active hemorrhage

Associated with high likelihood of continued HE

Associated with worse clinical outcomes and increased mortality

Sources: N Engl J Med. 2022 Oct; 387:1589-1596.
Stroke. 2007 April; 38(4):1257-1262

Intervention



Source: JAMA Neurol. 2019 Dec 1;76(12):1493-1501.

Baseline Characteristics

Variable	Placebo (N=37)	80 mcg/kg (N=32)
Age (yr)	66.7	70.7
Male (%)	54	47
White (%)	54	66
NIHSS	16	16
GCS	13	14
Mean ICH volume (mL)	20.4	16.3
Intraventricular hemorrhage (%)	38	44
Time from onset to treatment (min)	161	195
Treated <3 hr after onset (%)	65	37

Source: JAMA Neurol. 2019 Dec 1;76(12):1493-1501.

Efficacy & Safety Outcomes

Hematoma Expansion (mL Increase)		
Dose	**mL (IQR)**	**P-Value**
Placebo	2.6 (0 to 6.6)	-
80 mcg/kg	2.5 (0 to 10.2))	0.89

Survival at Day 90		
Dose	**No. (%)**	**P-Value**
Placebo	6 (21)	-
80 mcg/kg	7 (20)	0.98

Myocardial infarction, ischemic stroke, or pulmonary embolism		
Dose	**No. (%)**	**P-Value**
Placebo	4 (11)	-
80 mcg/kg	2 (6)	0.68

Source: JAMA Neurol. 2019 Dec 1;76(12):1493-1501.

Conclusion

Strengths

Pooled results from two trials with similar inclusion and exclusion criteria

Required use of spot sign on CT to determine if CT spot sign should be used in a treatment algorithm for patients presenting with ICH

Weaknesses

Allowed treatment up to 6 hr after onset of symptoms

Onset of ICH to treatment was significantly lower for placebo

Very small population (likely underpowered trial)

Conclusion

rFVIIa did not significantly reduce hemorrhage expansion in patients with spot sign–positive ICH when treated within 6.5 hours of onset

Source: JAMA Neurol. 2019 Dec 1;76(12):1493-1501.

Cochrane Meta-Analysis

Study Design

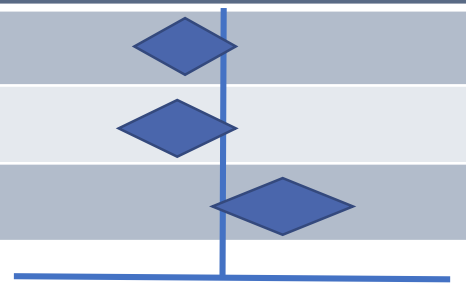
Meta-analysis of 12 RCTs involving 1732 patients

Factor VIIa: FAST, Phase 2b, Phase 2a, and 2 other trials

Objective

To examine the effectiveness and safety of individual classes of hemostatic therapies, compared against placebo or open control, in adults with acute spontaneous intracerebral hemorrhage

Outcome	No. (%) Intervention	No. (%) Control	RR (95% CI)	Forrest Plot
Death/Dependence	465 (48)	409 (51)	0.86 (0.66 to 1.11)	
Death at 90 Days	181 (18)	94 (21)	0.71 (0.44 to 1.14)	
TE Events	81 (8)	28 (7)	1.24 (0.8 to 1.91)	



FAVORS INTERVENTION FAVORS PLACEBO

Source: Cochrane Database Syst Rev. 2018 Apr 17;4(4).

OVERALL CONCLUSION

Role of rFVIIa in sICH

Current evidence does not suggest that rFVIIa has a role in sICH

Future trials are warranted to identify subgroups of patients that could potentially benefit from rFVIIa

Future Directions

FASTEST trial underway

Evaluating patients with sICH who have smaller baseline volumes of ICH and IVH

Within 120 minutes of stroke onset with a goal to treat ½ patients within 90 minutes

Utility

rFVIIa associated with high cost	Limited utility due to very specific population

ASSESSMENT QUESTION 3

According to the post-hoc analysis of the FAST trial, which patient would most likely benefit from the administration of factor VIIa after presenting with a spontaneous intracerebral hemorrhage?

a. 82-year-old male with symptom onset of 1 hour, ICH volume of ~55 mL, no IVH
b. 65-year-old male with symptom onset of 1 hour, ICH volume of ~45 mL, no IVH
c. 55-year-old female with symptom onset 3.5 hours, ICH volume of 45 mL, no IVH
d. 64-year-old male with symptom onset of 1 hour, ICH volume of ~55 mL, and IVH volume of ~10 mL

ASSESSMENT QUESTION 3 CORRECT RESPONSE

According to the post-hoc analysis of the FAST trial, which patient would most likely benefit from the administration of factor VIIa after presenting with a spontaneous intracerebral hemorrhage?

a. 82-year-old male with symptom onset of 1 hour, ICH volume of ~55 mL, no IVH
b. 65-year-old male with symptom onset of 1 hour, ICH volume of ~45 mL, no IVH
c. 55-year-old female with symptom onset 3.5 hours, ICH volume of 45 mL, no IVH
d. 64-year-old male with symptom onset of 1 hour, ICH volume of ~55 mL, and IVH volume of ~10 mL

ASSESSMENT QUESTION 4

True or false, patients presenting with spontaneous intracerebral hemorrhage with CT spot sign show improved outcomes after hemostatic agents are administered

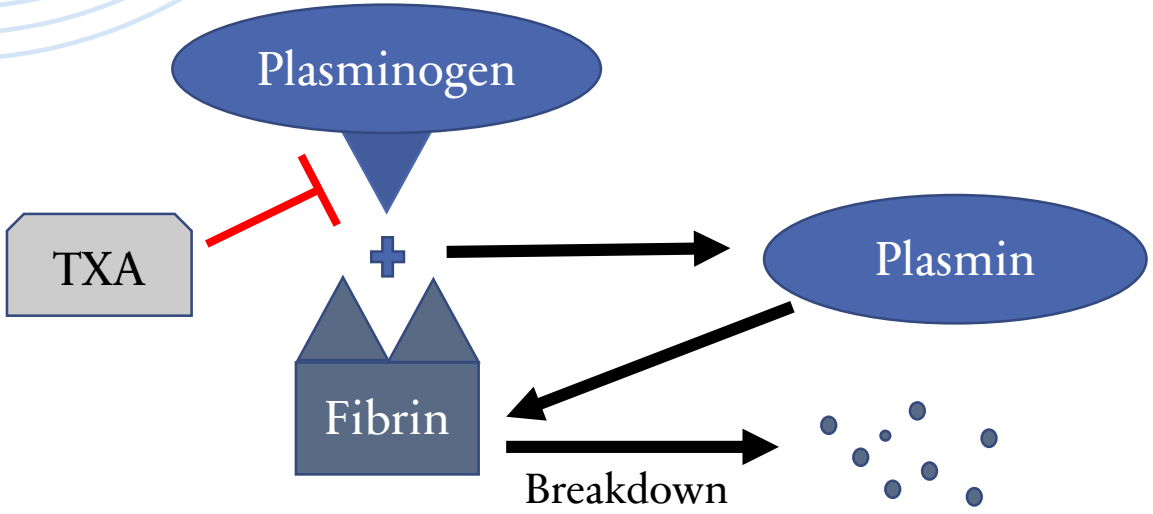
a. True
b. False

ASSESSMENT QUESTION 4 CORRECT RESPONSE

True or false, patients presenting with spontaneous intracerebral hemorrhage with CT spot sign show improved outcomes after hemostatic agents are administered

a. True
b. False

TRANEXAMIC ACID (TXA)



Mechanism of Action

Competitive inhibitor to receptor found on plasminogen → Prevents conversion of plasminogen to plasmin → Decreased fibrin breakdown

Rationale for Use in SICH

CRASH-2 and CRASH-3 Trial

TXA has shown benefit in bleeding trauma patients on mortality

CRASH-2 administered within 8 hr of injury
CRASH-3 within 3 hr of injury

Sources: Health Technol Assess. 2013 Mar;17(10):1-79.
Lancet. 2019 Nov 9;394(10210):1713-1723

TICH-2 Trial

Study Design	Multi-center, double-blind, randomized, placebo-controlled trial across 12 countries at 124 sites
Objective	To test the hypothesis that intravenous tranexamic acid reduces death and dependence when given within 8 h of spontaneous intracerebral hemorrhage

Inclusion

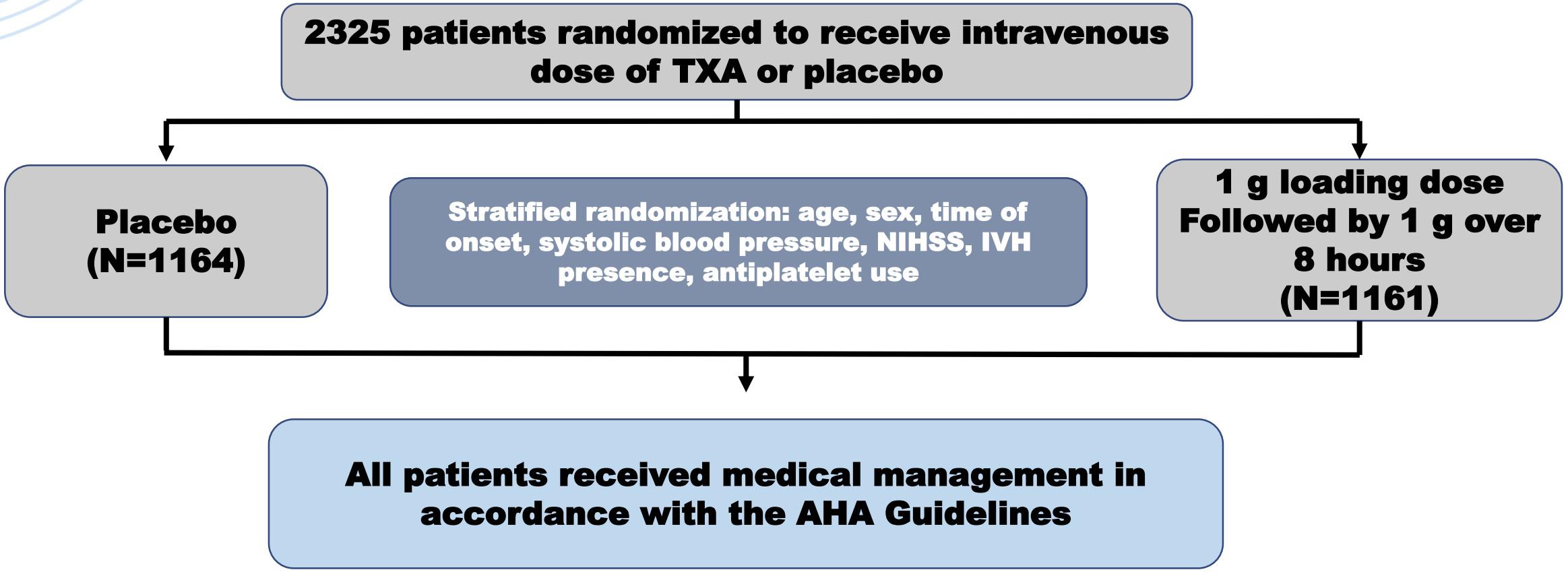
- ≥18 years of age
- CT scan of spontaneous intracerebral hemorrhage
- Symptoms onset within 8 hours
- GCS ≥5

Exclusion

- mRS >4 prior to ICH
- Life expectancy <3 months
- Oral anticoagulant use
- Any coagulopathy potential
- Any symptomatic thrombotic or vaso-occlusive disease within 30 days

Source: Lancet. 2018 May 26;391(10135):2107-2115.

Intervention



Source: Lancet. 2018 May 26;391(10135):2107-2115.

Baseline Characteristics

Variable	Placebo (N=1164)	TXA (N=1161)
Age (yr)	68.7	69.1
Male (%)	57	55
White (%)	85	85
Prior antiplatelet use (%)	25	27
Systolic blood pressure (mmHg)	174	172
ICH volume (mL)	12.5	14.1
IVH Presence (%)	31	33
Pre-stroke mRS	0	0
NIHSS	13	13
GCS	14	13
Time from onset to randomization		
≤3 hr (%)	35	36
≤4.5 hr (%)	68	67

Source: Lancet. 2018 May 26;391(10135):2107-2115.

Efficacy and Safety Outcomes

Shift in mRS Score at Day 90		
	Ordinal OR (95% CI)	P-Value
TXA vs. Placebo	0.88 (0.76 to 1.03)	0.11

Survival at 90 Days			
	No. (%)	HR (95% CI)	P-Value
Placebo	249 (21)	-	-
TXA	250 (22)	0.92 (0.77 to 1.1)	0.37

Hematoma Expansion			
	No. (%)	OR (95% CI)	P-Value
Placebo	304 (29)	-	-
TXA	265 (25)	0.8 (0.66 to 0.98)	0.03

Subgroup Analysis of mRS Shift		
	Mean Difference (95% CI)	P-Value
BP ≤ 170 mmHg	0.73 (0.59 to 0.90)	0.0188
Baseline Volume of 30-60 mL	0.66 (0.44 to 0.98)	-

Authors reported that patients who received TXA had lower rates of serious adverse events. There was not a significantly higher rate of arterial occlusion or venous thromboembolism (3% in both groups)

Source: Lancet. 2018 May 26;391(10135):2107-2115.

CONCLUSION

Strengths	Well balanced baseline characteristics Broad inclusion criteria
Weaknesses	Allowed enrollment up to 8 hours after onset Smaller population when compared to other TXA trials (Possibly underpowered to detect clinical outcomes)

Author's Conclusion

- TXA did not affect functional status or mortality at day 90
- Future research should investigate which subgroups of patients might benefit

Source: Lancet. 2018 May 26;391(10135):2107-2115.

META-ANALYSIS

Study Design

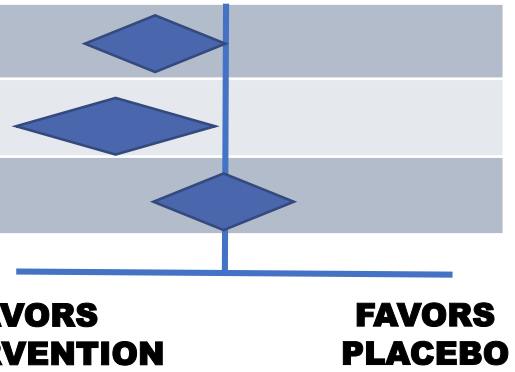
Meta-analysis of 4 RCTs involving 2666 patients with high risk hemorrhage growth (CT spot, black hole, and blend sign)

3/4 RCTs were TXA and 1/4 RCTs was rFVIIa

Objective

To evaluate the effect of hemostatic agents on the prevention of hemorrhage growth in patients with high-risk, spontaneous ICH

Outcome	Placebo (%)	Intervention (%)	OR (95% CI)	Forrest Plot
HE	**40**	**27.4**	0.84 (0.7 to 1.00)	
HE with black hole sign	-	-	0.61 (0.39 to 0.94)	
Dependence/Death	**53.3**	**53.3**	1.00 (0.86 to 1.17)	



Source: Stroke Vasc Neurol. 2021 Jun;6(2):170-179.

OVERALL CONCLUSION OF TXA

Role of TXA in sICH

Current evidence does not suggest that TXA has a role in sICH

Future trials with larger sample sizes are warranted to potentially identify a modest clinical benefit in TXA

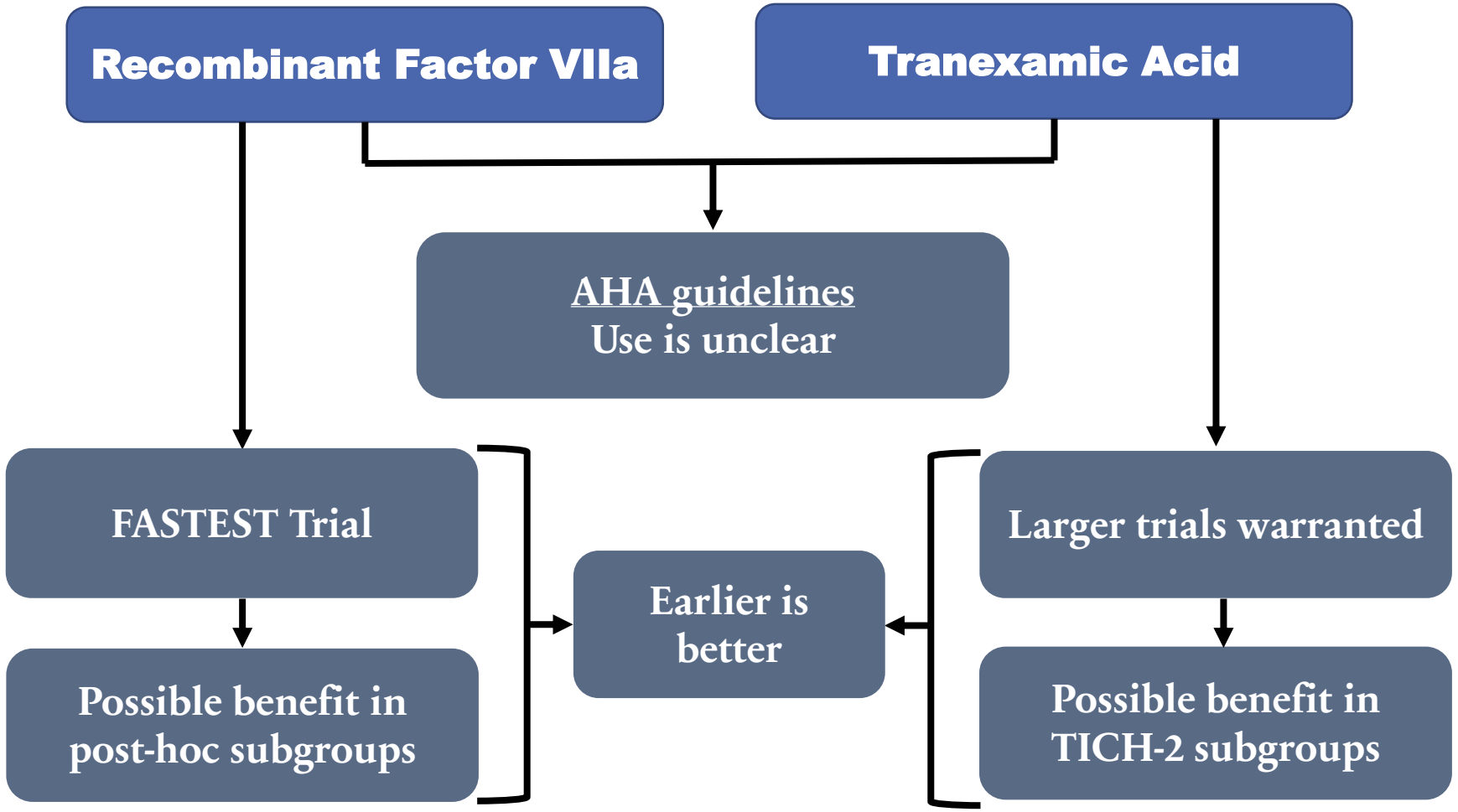
Utility

Better safety profile than Factor rVIIa

Widely available

Low cost

GENERAL HEMOSTASIS



Stroke. 2022;53:e282–e361.

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THANK YOU!

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