Establishing AIS Best Practice and Standards Through Evidence Based Medicine

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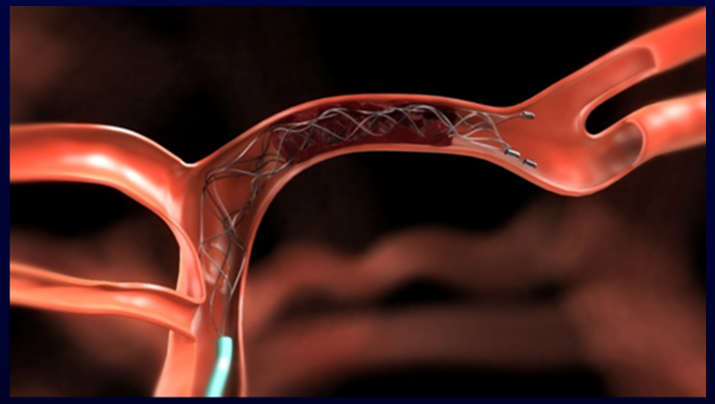

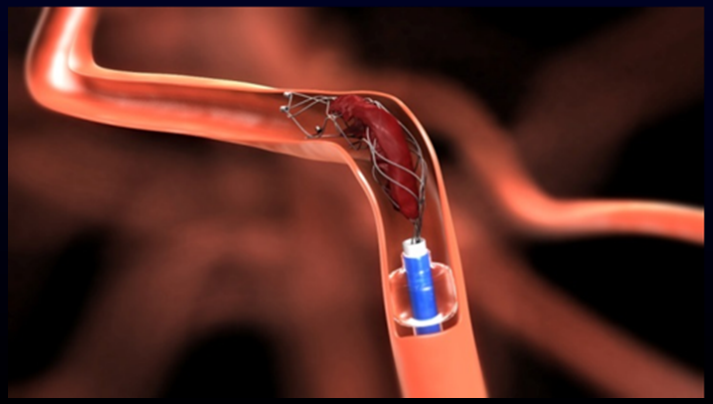

Disclosures:

Covidien/ EV3

Consultant, Speaker

Stryker Neurovascular/ Surpass

Consultant/Stock Holder

Codman Neurovascular

Consultant, Speaker

Agenda

1. Stent Retriever Trial Review
2. European Multicenter Prospective Data (STAR)
3. North American Multicenter Retrospective Data (NASA)
    - Technical Considerations – Balloon Guide Catheter
4. Stentriever Single Center Device Outcome Data
5. Summary

STAR: Solitaire™ FR Thrombectomy For Acute Revascularization

Study Design

Study Design Summary	
Study Type	Single arm, multicenter, International trial of Solitaire™ FR device used in routine practice
Objective	This clinical evaluation is a multi-center, single-arm, prospective, observational evaluation of the treatment with a mechanical revascularization device for patients diagnosed with an acute ischemic stroke.
Population	Treatment of patients with Acute Ischemic Stroke within 8 hrs of symptom onset
Target Vessel	Anterior Circulation (M1 or M2, ICA and ICA Terminal)
Randomization	Non-randomized single arm clinical study (SFR)
Sites	14 EU centers, 1 Canada, 1 Australia
Sample Size	202 Patients
Follow-up	24-48hrs, 7-10 days or D/C, and 90-day

Study Design

Study Endpoints	
Primary Endpoints	Arterial recanalization of occluded target vessel measured by TICI score following the final recovery of Solitaire™ FR device within 3 passes.
Secondary Endpoints	• Time to revascularization • Measurement of patient's neurological condition including NIHSS and • mRS at 90 days post procedure • Rate of morbidity and mortality • Incidence of symptomatic intracranial hemorrhage • Immediate flow reperfusion
Safety	Incidence of device-related and procedure related Serious Adverse Events
Health Economics	Not applicable

Inclusion Criteria

- Age ≥ 18 and < 85
- Clinical signs and imaging criteria consistent with acute ischemic stroke
- NIHSS ≥ 8 and ≤ 30
- TICI 0 or 1 in proximal anterior intracranial vasculature (M1 or M2 of MCA, ICA intracranial, ICA terminal)
- Presentation within 8 hours of stroke onset according to local stroke protocol
- If stroke presentation within 4.5 hours, one of these conditions can be met:
  - Bridging protocol (starting IV and continuing with IA) (up to max 0.9 mg/kg)
  - Failed IV thrombolysis
  - Direct IA treatment (according to institution guidelines)
- mRS ≤ 2 prior to stroke onset
- Willing to conduct follow-up visits
- Signed ICF from patient or LAR (if required)

Exclusion Criteria

- Pregnant or lactating
- Known serious sensitivity to radiographic contrast agents
- Rapidly improving neurological signs
- Current participation in another investigational drug/device study
- Life expectancy of less than 90 days
- NIHSS > 30 or coma
- Uncontrolled hypertension: SBP > 185 or DBP > 110 that cannot be controlled except with continuous parenteral antihypertensive medication
- Use of warfarin with INR > 3.0
- Platelet count < 30,000
- Glucose >400 mg/dL
- Previous stroke within 30 days
- Unknown time of symptom onset
- Seizure at stroke onset
- Myocardial infarction or infection (sepsis or endocarditis)
- Arterial tortuosity that would prevent device from reaching target vessel
- Known hypersensitivity to nickel-titanium

Imaging Exclusion Criteria

- Angiographic evidence of carotid dissection, complete cervical carotid occlusions, or vasculitis
- Stenosis proximal to thrombus site that may preclude safe recovery of the device
- Brain CT with signs of hemorrhage, AVM or aneurysm
- Early ischemic changes > 1/3 of the middle cerebral artery (MCA) territory or according to brain CT ASPECTS score ≤ 6 or according to MR DWI ASPECTS score < 5

Study Endpoints

Primary Efficacy	Arterial recanalization of the occluded target vessel measured by TICI ≥ 2b following the use of no more than three passes of the study device Successful recanalization = achieving TICI 2b or 3 flow for the target territory, includes: •Intracranial ICA •ACA •MCA (all M1 and M2 segments) •Internal carotid terminus lesions and both M2 branches
Safety	Incidence of device-related and procedure-related serious adverse events
Secondary	1) Neurological condition including NIHSS and mRS at 90 days post procedure 2) Rate of morbidity and mortality at 90 days post procedure 3) Incidence of symptomatic intracranial hemorrhage 4) Time to revascularization 5) Immediate Flow Reperfusion

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Protocol Violations by Inclusion/Exclusion (CEC, Core Lab, Clinical)

Protocol Violation	N
ASPECTS	20
Life Expectancy	3
Other (pregnant, labs)	2
Unk onset time	2
Uncontrolled HTN	2
Age (>85)	1
Carotid Dissection	1
Tortuosity	1
mRS >2	1
Occlusion Location (m3)	1
Stroke <30days	1
Total	**35**

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Stroke Presentation (cont.)

ASPECTS Pre-Procedure as per Core lab	CT imaging at baseline	MR imaging at baseline	Total
3	1% (1/147)	2% (1/52)	1% (2/199)
4	1% (2/147)	8% (4/52)	3% (6/199)
5	3% (5/147)	23% (12/52)	9% (17/199)
6	5% (7/147)	2% (1/52)	4% (8/199)
7	16% (23/147)	17% (9/52)	16% (32/199)
8	34% (50/147)	33% (17/52)	34% (67/199)
9	20% (30/147)	13% (7/52)	19% (37/199)
10	20% (29/147)	2% (1/52)	15% (30/199)
Note: 3 patients missing ASPECTS (10-0004, 12-0021, and 19-0004)			

Chi-square p<0.001 between groups

Patient and Stroke Characteristics

Characteristic	Result
Median Age	72 (25.0, 86.0)
Male	40% (80/202)
Baseline NIHSS, median	17
Time to Treatment, median, Mean	250 minutes (94, 723) 266 ± 98 (196)

Patient and Stroke Characteristics

Occluded Vessel (per Angiographic Core Lab)	
Cervical ICA	0% (0/196)
ICA Terminal	18% (36/196)
MCA	82% (160/196)
M1	67% (131/196)
M2	14% (28/196)
M3	0.5% (1/196)

Note:
Core lab missing "vessel treated" for 6 subjects: 008-0005, 012-0002, 017-0002, 017-0004, 019-0010, and 019-0012

Primary Endpoint (TICI)

Post Procedure TICI		
TICI	**N**	**%**
0	7	3.6%
1	0	0.0%
2a	16	8.3%
2b	60	30.9%
3	111	57.2%
Total	**194**	

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Procedure Characteristics

Characteristic	Result Median (min, max) Mean ± SD (N)
Number of Passes	1.0 passes (1.0, 3.0), 1.5 ± 0.7 (202)
Time from Stroke Onset to Groin Puncture (min)	238 minutes (72, 714) 251 ± 99 (195)[1]
Time from Groin Puncture to Balloon Catheter in Place (min)	12 (1, 62) 15 ± 10 (193)[2, 3]
Time from Balloon Catheter in Place to TICI 2b/3 or Final DSA (min)	20 (1, 157) 29 ± 27 (194)[4]

1. Missing Time from Stroke Onset to Groin Puncture for 7 subjects: 007-0003 (missing stroke onset time); 007-0019, 012-0004, 012-0006, 012-0007, 016-0010, 016-0011 (missing groin puncture time)
2. Five subjects missing Balloon Catheter Time (012-0004, 012-0005, 012-0006, 012-0007, 020-0007). BGC was used in all 5 cases, however, time of placement was not documented.
3. Missing Time from Groin Puncture to Balloon Catheter placement for 8 subjects: 007-0019, 016-0010, 016-0011 (missing groin puncture time only); 012-0004, 012-0006, 012-0007 (missing both groin puncture time and balloon catheter time); and 012-0005, 020-0007 (missing balloon catheter time only); 2 data points excluded due to erroneous entry
4. Missing Time from Balloon Catheter placement to Final DSA for 8 patients: 5 subjects *noted above* (missing balloon catheter time); 012-0016, 016-0006, and 016-0007 (missing Final DSA time); 1 data point excluded due to erroneous entry

Secondary

Clinical Outcomes

Criteria	Result
mRS ≤ 2 at 90 days	57.9% (117/202)
Mortality at 90 days	6.9% (14/202)

Secondary

Hemorrhagic Transformation Outcomes

Criteria	Result	
All ICH within 24 hrs of procedure per CEC adjudication	18.8% (38/202)[1]	
Type of ICH[2]	***# of Events***	***# of Subjects***
HI1	*19*	*19*
HI2	*10*	*10*
PH1	*6*	*6*
SAH	*6*	*6*
IVH + PH2	*1*	*1*
SICH[2] per CEC adjudication	1.5% (3/202)	

1. Column for # of subjects does not sum due to multiple categories per patient.
2. Symptomatic intracranial hemorrhage defined as any PH1, PH2, RIH, SAH, IVH associated with NIHSS score increase ≥ 4 within 24 hrs.

Safety

Device Related SAE: adjudicated by independent CEC

Relationship	Result % (n/N) [AEs]
Device Related: Ancillary SAEs	0.5% (1/202) [1]
Device Related: Solitaire™ FR SAEs • Vessel dissection (2) • Embolus to uninvolved territory (2) • Intracranial hemorrhage (2)	2.5% (5/202) [6]
Device Related: Unknown SAEs	0.5% (1/202) [1]

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Procedure/Treatment related SAE: adjudicated by Independent CEC

Safety

Relationship	Result % (n/N) [AEs]
Procedure/Treatment Related SAEs • Ischemic stroke (3) [2 recovered with sequelae / 1 died] • Access site occlusion (1) [recovered without sequelae] • Access site hematoma (2) [2 recovered without sequelae] • Access site pseudoaneurysm (1) [recovered without sequelae] • Worsening of stroke (1) [subject died] • Vessel perforation (1) [recovered without sequelae] • ICA dissection (1) [recovered without sequelae] • Aspiration pneumonia (1) [subject died]	5.4% (11/202) [11]
All device- and/or procedure-related SAEs	7.4% (15/202) [19]

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Core Lab Reviewed MT Clinical Trials - Results

	Retrospective*	SWIFT **,**** (Rand SFR group only)	TREVO***	TREVO 2 *** (Rand Trevo group only)
N	141	58	60	88
Age	66.3 ± 13.1	67.1 ± 12.0	65 (median)	67.4 ± 13.9
Male	56% (79/141)	48% (28)	45%	45%
Baseline NIHSS, median	18	18	18	19
% ICA occlusions	28%	21%	21.7%	16%
% VBA occlusions	11%	1.7%	8.3%	8%
Successful recanalization	85% (TICI ≥2b)	68.5% (TIMI ≥2) 75.9% (TICI ≥2b)	78.3% (TICI ≥2a)	86% (mTICI≥2)
mRS ≤ 2 at 3 months	55% (77/141)	36.4% (20/55)	55.0%	40%
Mortality at 3 months	20% (20/141)	17.2% (10/58)	20%	33%
Symptomatic ICH at 24 hrs	4% (5/141)	1.7% (1/58)	5% (3/60)	7%

*Dávalos A, Mendes Pereira V, Chapot R, et al; Retrospective Multicenter Study of Solitaire FR for Revascularization in the Treatment of Acute Ischemic Stroke. *Stroke. 2012;43:2699-2705.*

****Abstract 163: TICI Success Rates In Swift: Comparison Between Randomized Arms And Correlation To 90 Day Neurologic Outcome. Jahan, et. al. Presented at ISC 2013

T****revo Versus Merci Retrievers for Thrombectomy Revascularisation of Large Vessel Occlusions in Acute Ischaemic Stroke (TREVO 2): a randomised trial. Nogueira et. al., *doi:10.1016/S0140-6736(12)61299-9.*

S**aver J, Jahan R, Levy E, et al; SWIFT Trialists. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet. 2012;380(9849):1241-1249.*

Solitaire™ FR: North American Multicenter Retrospective Data (NASA)

Zaidat OO, Castonguay AC, Gupta R, Sun CJ, Martin CO, Holloway WE, Mueller-Kronast N, Malisch TW, Marden FA, Bozorgchami H, Xavier A, Rai A, Badruddin A, Taqi MA, Linfante I, Dabus G, Abraham MG, Shaltoni H, Janardhan V, Nguyen TN, Abou-Chebl A, Chen PR Yoo AJ, Britz GW, Kaushal R, Nanda A, Issa M, Nogueira R
for the NASA investigators, USA

NASA Registry

- NASA Registry 20 sites in North America
- Acute stroke patients treated with the SOLITAIRE FR
- Symptomatic intracranial hemorrhage (sICH) was defined as any parenchymal hematoma, SAH, or IVH associated with a worsening of the NIHSS score by≥4 within 24 hours
- The primary outcome was achieving TIMI≥2 or TICI≥2a revascularization
- Secondary outcomes were mRS at 3 months, mortality, and sICH. The data was housed and analyzed by a central coordinating site, the Medical College of Wisconsin

NASA Registry

- 354 patients underwent treatment for acute ischemic stroke using the SOLITAIRE FR
- Mean age of 67.3 ± 15.2; Median of 70 (IQR 55-79)
- Equally divided between women 49.6% (178/354), with majority white 74% (250/354)
- Median baseline NIHSS was 18 (IQR 14-22)
- Mean time from onset to groin puncture was 363.4±239 minutes; mean fluoroscopy time of 32.9±25.7 minutes
- mean procedure time of 100.9±57.8 minutes

North American Solitaire Stent-Retriever Acute Stroke Registry (NASA) – Baseline Characteristics

Investigator-initiated registry: 354 AIS treated with Solitaire FR b/w March 2012 and Fe

Characteristics	NASA (n=354)	SWIFT (n=58)	P-value NASA vs SWIFT	TREVO 2 (n=88)	P-value NASA vs TREVO 2
Age, y; Mean (SD)	67.3 (15.2)	67.1 (12.0)	0.9	67.4 (13.9)	0.9
Sex (% male)	178 (50.4%)	52%	0.9	55%	0.5
Atrial fibrillation	148 (42%)	45%	0.7	48%	0.4
DM	87 (25%)	24%	0.9	38%	0.05
HTN	271 (77%)	72%	0.4	76%	0.8
Hyperlipidemia	182 (52%)	53%	0.9	63%	0.1
Smoking History	108 (31%)	40%	0.2	42%	0.11
CAD	111 (32%)	33%	0.9	33%	0.9
Baseline NIHSS, Mean (SD)	18.1 (6.6)	17.3 (4.5)	0.3	18.3 (5.3)	0.6
MCA/M1	197 (56%)	66%	0.2	60%	0.6
ICA terminus	82 (23.2%)	21%	0.7	16%	0.2
Basilar*	36 (10.2%)	2%	0.05	8%	0.6
Time of onset to groin puncture (TOG), min, h, Mean (SD)*	363.4(239) 6.1 (4)	301.6(71.2) 5 (1.2)	<0.001	276 (90) 4.5 (1.5)	<0.001
Time to revascularization or end of procedure, min: Median (IQR), or	50 (30.8-78.8)	36 (18-65)		NA	
mean (SD)*	77 (96.3)	NA		47.8 (44.2)	<0.001

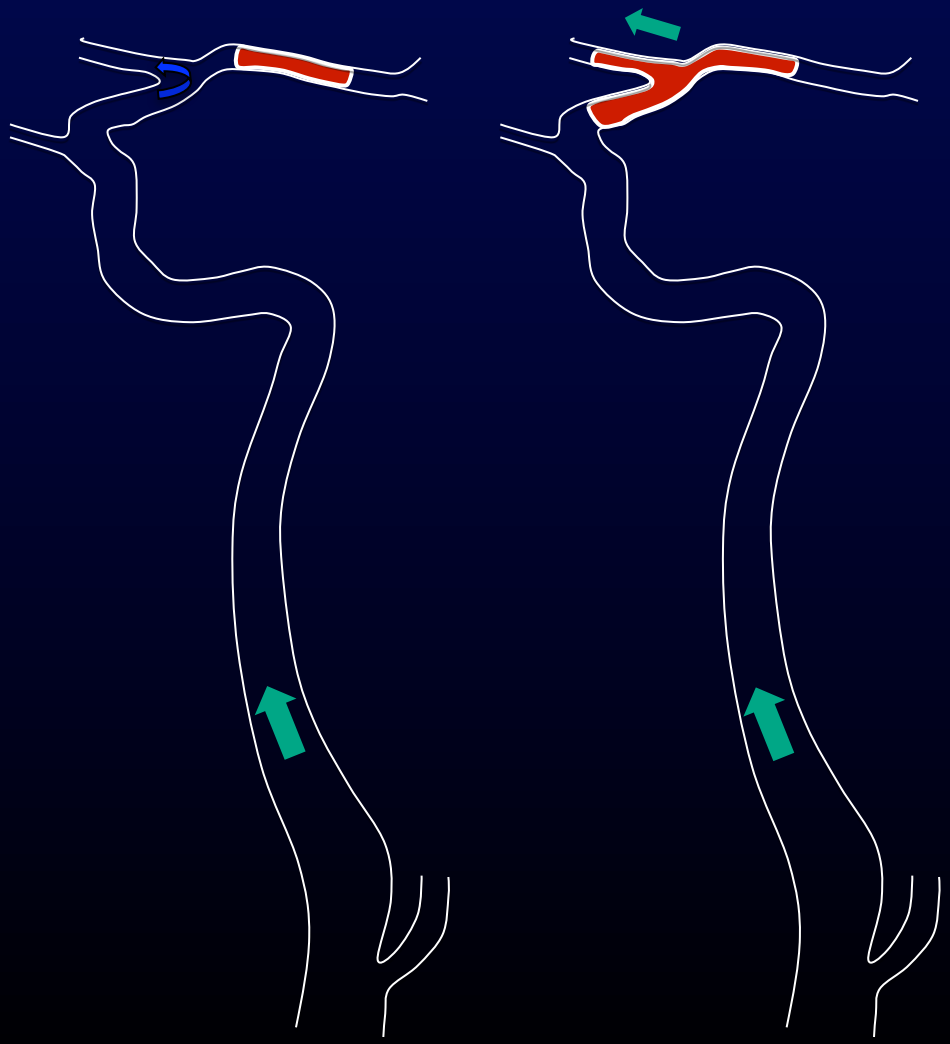
NASA – Revascularization and Clinical Outcomes

Outcome	NASA: (n=354)	SWIFT (58)	P-value	TREVO 2 (n=88)	P-value
TIMI ≥ 2	296 (83.3%)	83%	0.9	NA	NA
TICI ≥2a	310 (87.5%)	NA	NA	85%	0.5
TICI≥2b	256 (72.5%)	NA	NA	68%	0.4
TICI 3	142 (40.2%)	NA	NA	14%	<0.001
Rescue therapy	91 (25.7%)	21%	0.7	18%	0.2
Passes:					
1	172 (49%)				
2	94 (27%)				
3	64 (18%)				
More than 3 passes	6.3%: 4 in 14 (4.2%), 5 in 7 (2.1%) 9 in 1 (.03%)				
Mean (SD)	1.9 (1.1)	1.7 (0.9)	0.13	2.4 (1.4)	0.002
Median (IQR)	2 (1-2)	NA	NA	NA	NA
mRS ≤ 2	132/315 (42%)	37%	0.4	40%	0.5
Death	95/315 (30.2%)	17.2%	0.05	29%	1
sICH	35/352 (9.9%)	2%	0.05	4%	0.1

NASA – Independent Predictors of Good Outcomes

Variable	P-Value
Age	<0.001*
Hypertension	0.0476
Atrial fibrillation	<0.0001*
NIHSS initial	0.0088*
Site	0.08
IV tPA	<0.0001*
Time onset to groin or 1st angio	0.45
TIMI Success	0.25
Balloon Guide Cath	<0.0001*
General Anesthesia	0.026
Procedure time	0.06

Balloon Guide Catheter



Risk of thromboembolic events

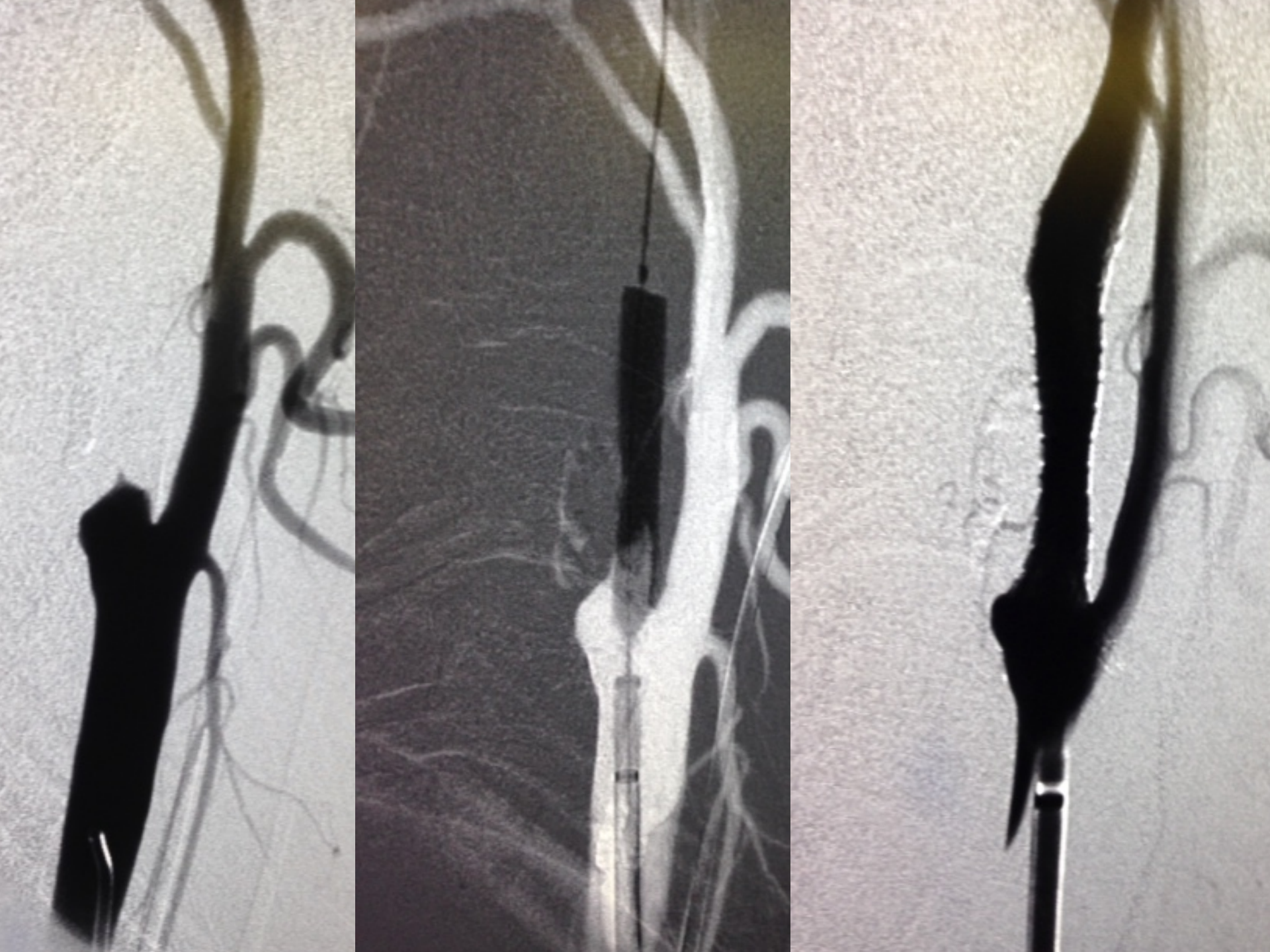
NASA Balloon Guide Catheter (BGC)

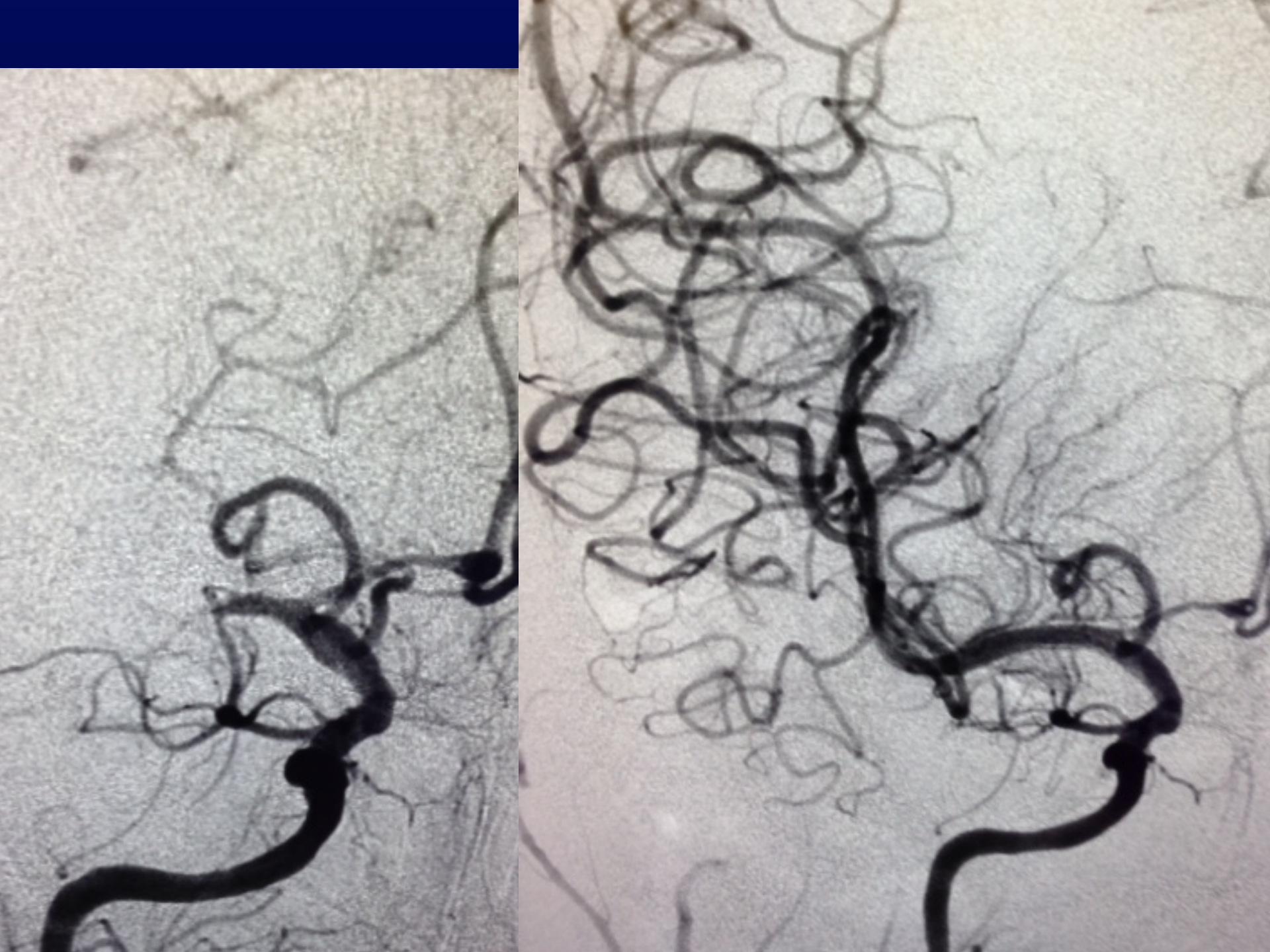
	Balloon Guide Catheter (N=149) N (%)	No Balloon Guide Catheter (N=189) N (%)	P Value
Imaging Results			
Emboli in new territory	8 (5)	10 (5.2)	0.9
Recanalization TICI3	**80 (53.7)**	**61 (32.5)**	<0.0001
Recanalization TICI2b-3	113 (76)	133 (71)	0.3
Procedural factors			
Procedure time (SD)	**120 (28.5)**	**161 (35.6)**	0.02
Time onset to groin or first angio (SD)	348 (230.7)	375 (252.7)	0.3
General anesthesia	97 (84.4)	99 (60)	<0.001
Number of passes (mean, SD) (Median, IQR)	1.8 (1.2) 1 (1-2)	1.9 (1) 2 (1-3)	0.3
IA tPA	40 (26.9)	60 (31.8)	0.3
Simultaneous Penumbra & Solitaire	18 (12.1)	34 (18.1)	0.1
Rescue therapy	**29 (20)**	**54 (28.6)**	0.05
Clinical Outcome			
Discharge NIHSS Mean (SD) Median (IQR)	 **12 (14.5)** **6 (1-18)**	 **17.5 (16)** **11 (4-42)**	0.002
Good clinical outcome (3 months)	**65 (51.6)**	**62 (35.8)**	0.02
Symptomatic hemorrhage	18 (12.2)	17 (9)	0.4
Mortality	33 (26.2)	55 (31.8)	0.3

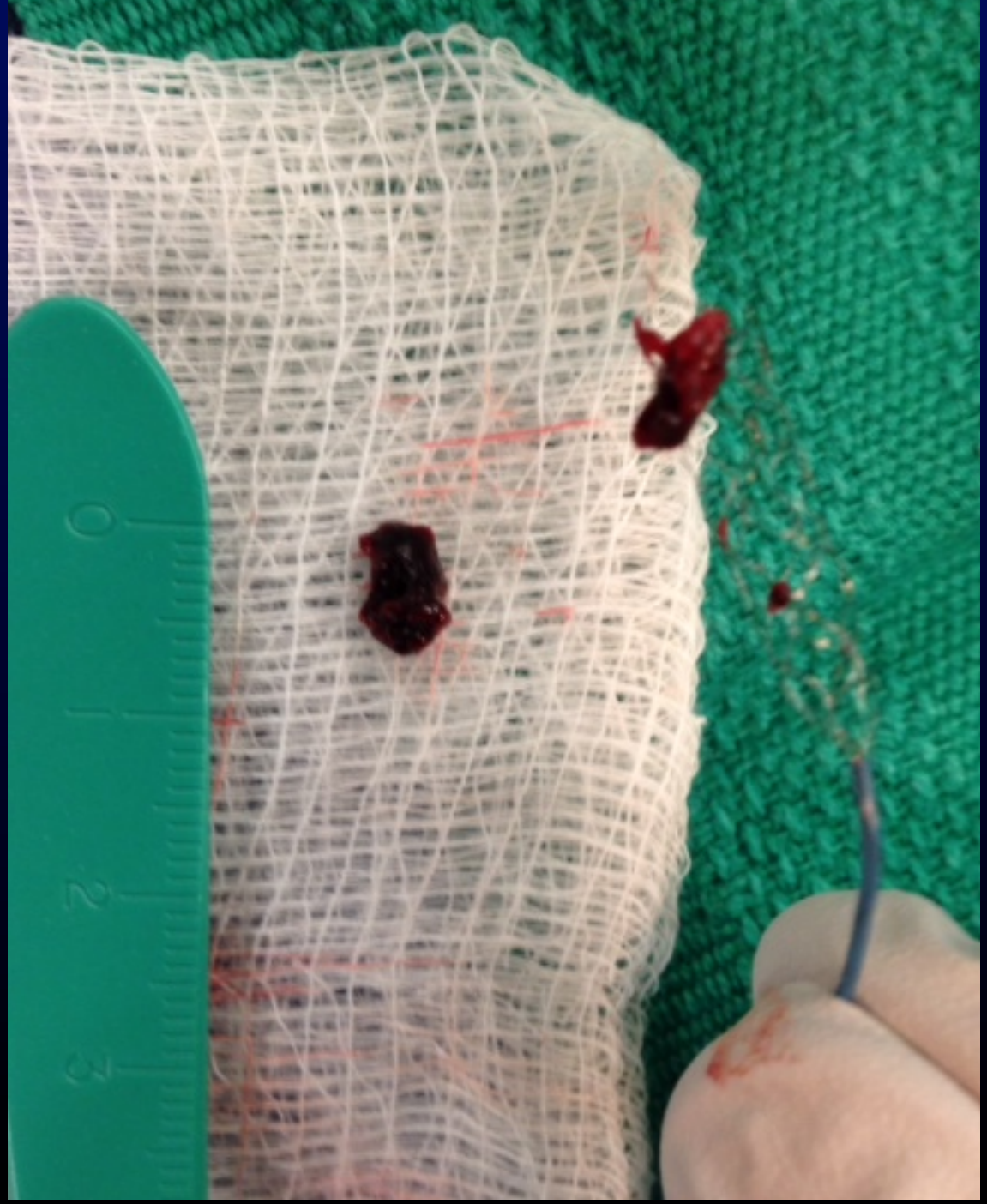
Nguyen T et al. NASA Sub analysis,

Patient

- 65 y/o man presenting with left hemiplegia, profound neglect, head and eye deviation (NIHSS 18)
- Decreased level of consciousness
- Intubated for airway protection
- IV tPA
- Cerebral Angiogram started 4-hours after symptom onset





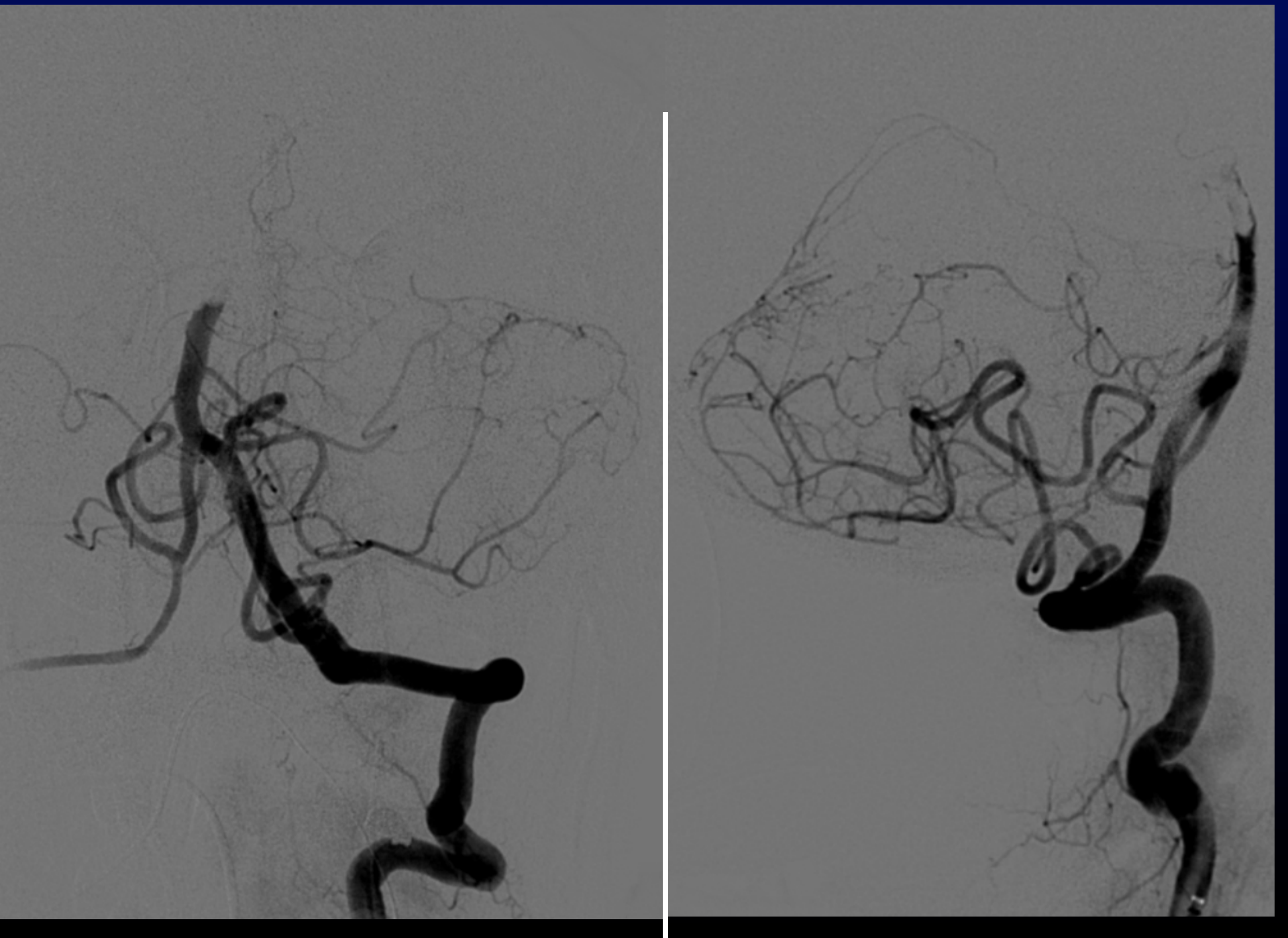


Patient

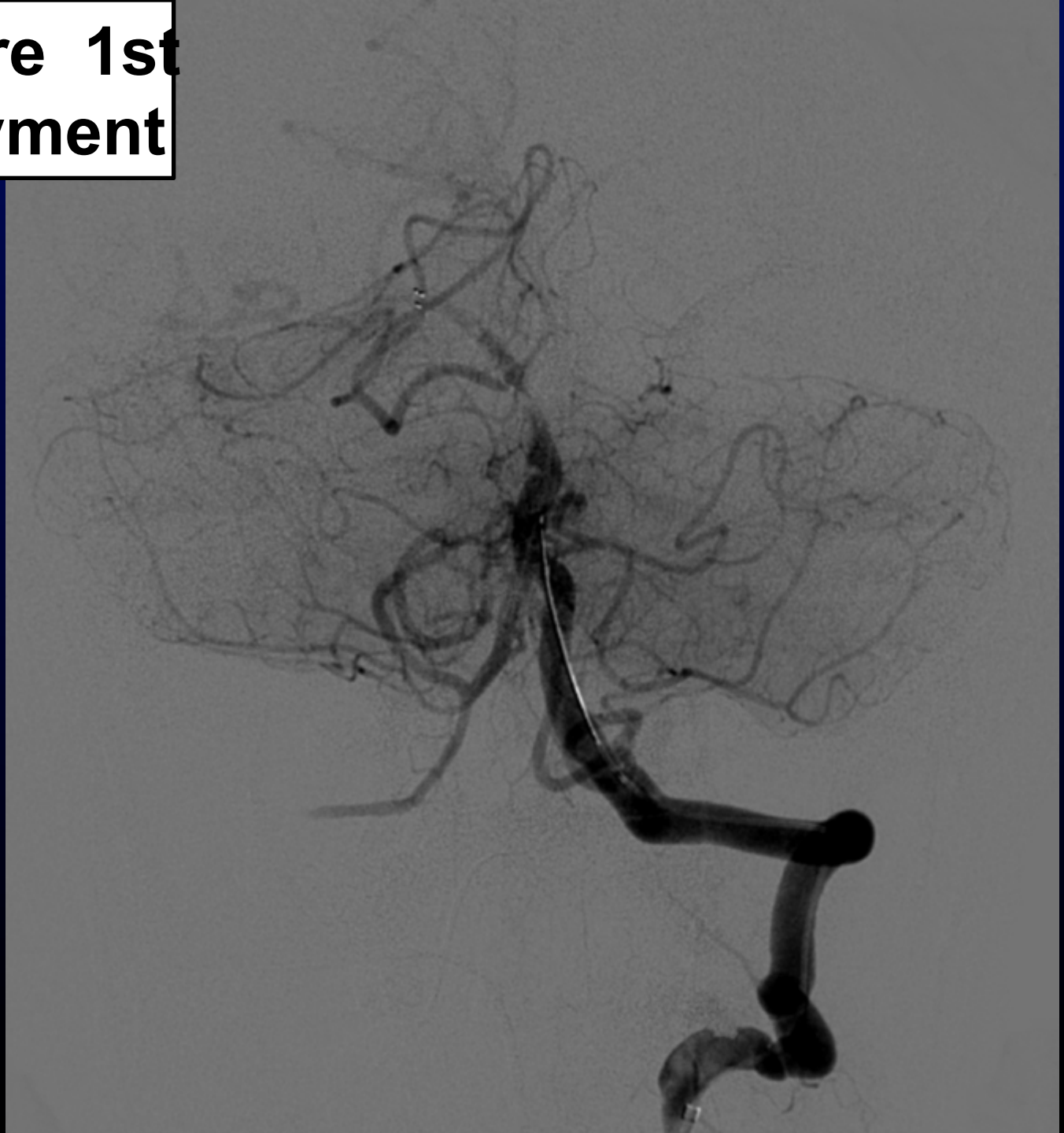
- Extubated the day after
- NIHSS of 2
- Home 4 days later

Patient

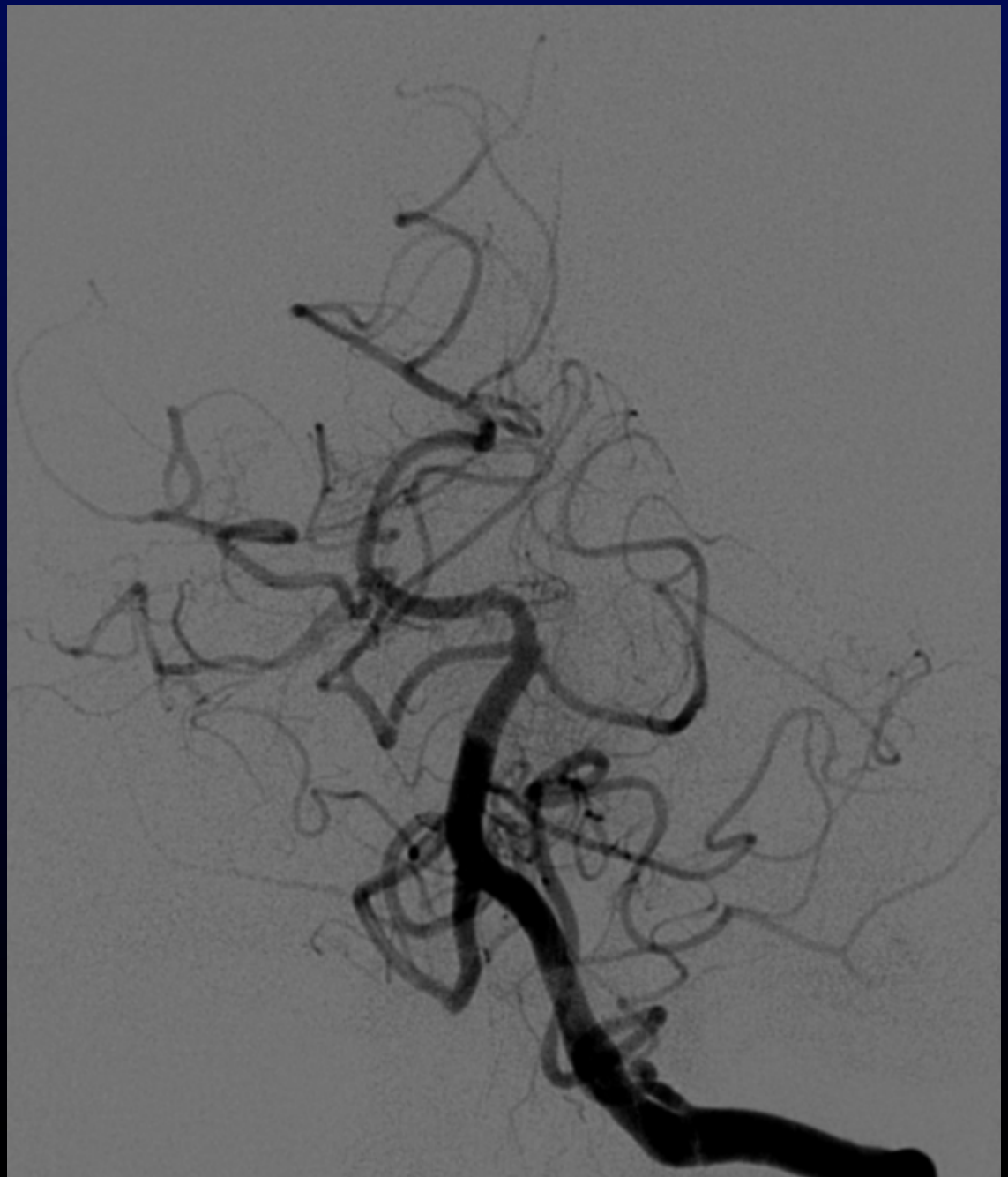
- 54 y/o man presenting with right hemiplegia, aphasia and INO (NIHSS 18)
- Top of the basilar artery occlusion on CTA
- No IV tPA due to recent STEMI
- Cerebral Angiogram started 4-hours after symptom onset



Solitaire 1st Deployment



Final Angiogram after two passes of Solitaire



Patient

- Extubated the day after
- NIHSS of 4
- Home 5 days later

Conclusions

Key interventional predictors of good neurological outcome

1. Use of a stent retriever device as first line therapy
2. Use of a balloon guide catheter
3. Procedural speed to TICI 3 recanalization

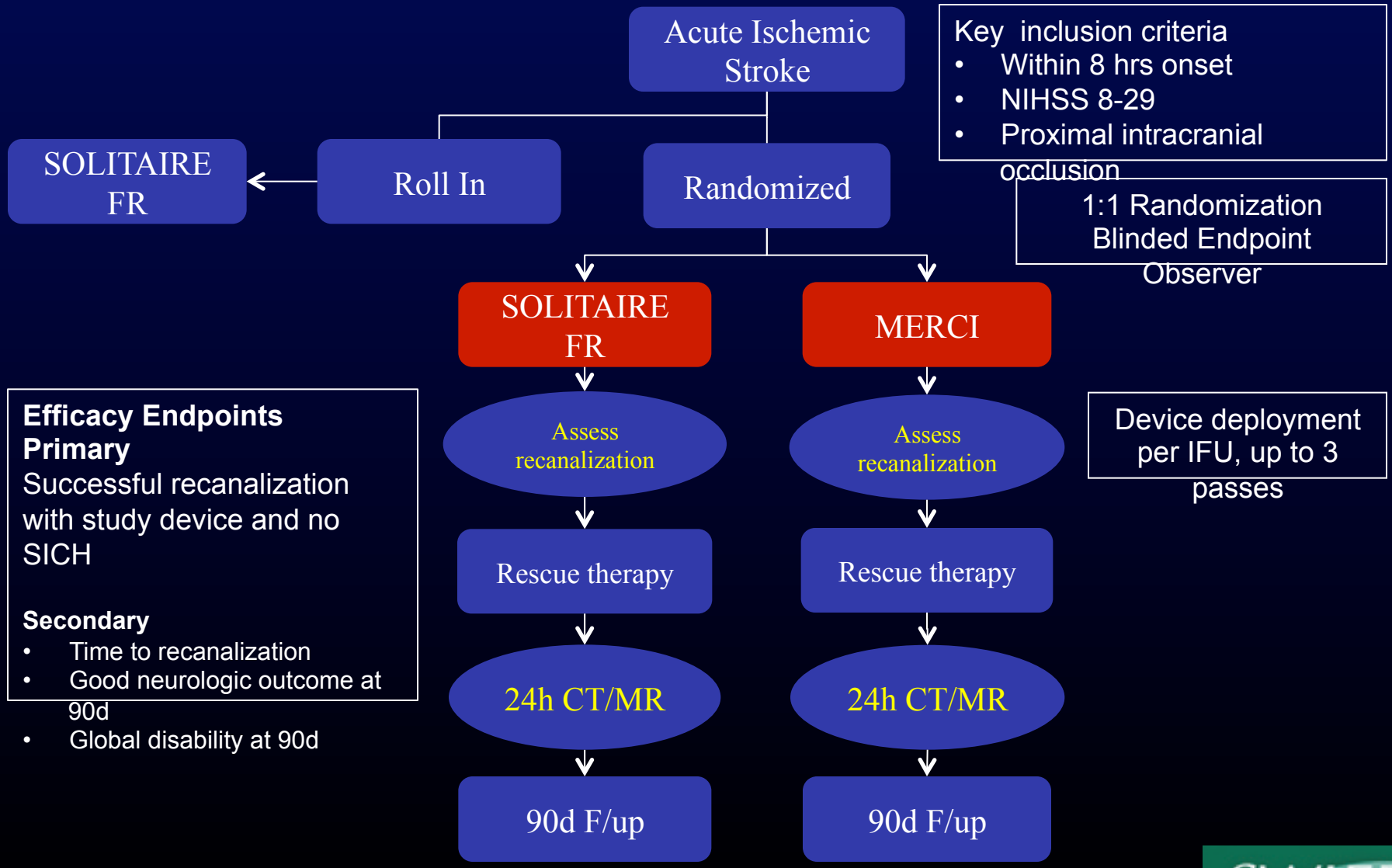
Key pre-interventional predictors of good neurological outcomes

1. Speed to Intervention: ASPECTS score >7 AND Incoming NIHSS
2. Use of IV-TPA prior to intervention
3. Local anesthesia

Q&A

Solitaire™ FR: North American Multicenter Prospective Data (SWIFT)

SWIFT Trial Design



Saver J, Jahan R, Levy E, et al; SWIFT Trialists. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet.*

SWIFT IDE Clinical Trial

SWIFT Trial: Baseline Features

Subject Characteristic	Roll-in (Solitaire FR) N=31	Randomized Solitaire FR N=58	Randomized Merci N=55	P value (rand)
Age	65.4 ± 14.5	67.1 ± 12.0	67.1 ± 11.1	0.99
Male	41.9% (13/31)	48.3% (28/58)	50.9% (28/55)	0.85[1]
NIHSS (mean) [median] (min, max)	17.5 ± 4.6 [18] (8, 26)	17.3 ± 4.5 [18] (9, 28)	17.5 ± 5.1 [18] (8, 26)	0.84
Pre-stroke Rankin (mean) [median] (min, max)	0.5 ± 1.2 (25) [0] (0, 4)	0.5 ± 0.8 (44) [0] (0, 3)	0.5 ± 1.0 (51) [0] (0, 5)	0.48[2]
BMI	29.9 ± 9.4	29.3 ± 6.8	29.4 ± 5.5	0.91
IV TPA Failure	67.7% (21/31)	34.5% (20/58)	47.2% (25/53)	0.18[1]
Time to First Diagnostic Angiogram (min)	284.8 ± 70.7	277.5 ± 85.2	297.7 ± 87.8	0.22

1. Fisher's Exact test 2. Wilcoxon's rank-sum

Saver J, Jahan R, Levy E, et al; SWIFT Trialists. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet.*

SWIFT IDE Clinical Trial

SWIFT Trial: Baseline Features

Subject Characteristic	Roll-in (Solitaire FR) N=31	Randomized Solitaire FR N=58	Randomized Merci N=55	P value[1] (rand)
MI	35.5%	32.8%	34.5%	0.85
HTN	54.8%	72.4%	69.1%	0.84
DM	32.3%	24.1%	30.9%	0.53
Hyperlipidemia	51.6%	53.4%	56.4%	0.85
Smoker	35.5%	39.7%	40.0%	1.00
Atrial Fibrillation	38.7%	44.8%	67.3%	0.02
PAD	9.7%	1.7%	7.3%	0.20
Past Ischemic Stroke	9.7%	13.8%	18.2%	0.61
Past Hem Stroke	3.2%	1.7%	9.1%	0.11
Past TIA	16.1%	5.2%	5.5%	1.00

1. Fisher's Exact test

Saver J, Jahan R, Levy E, et al; SWIFT Trialists. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet.*

SWIFT IDE Clinical Trial

SWIFT Trial: Primary Endpoint

Outcomes Among Randomized Patients	Randomized Solitaire FR N=58	Randomized Merci N=55	Non-inferiority P value[1]	Superiority P value[1]
Successful recanalization without SICH[2] (Core Lab)	**60.7% (34/56)**	**24.1% (13/54)**	**<0.0001**	**0.0001**
Successful recanalization study device **(Core Lab)**	68.5% (37/54)	30.2% (16/53)	<0.0001	0.0001
Successful recanalization study device (Site Assessed)	**83.3% (45/54)**	**48.1% (26/54)**	**<0.0001**	**0.0002**
Use of rescue therapy	20.7% (12/58)	43.6% (24/55)	<0.0001	0.015
End of procedure successful recanalization **(Site)**	88.9% (48/54)	67.3% (37/55)	<0.0001	0.010
End of procedure successful recanalization **(Core Lab)**	80.4% (45/56)	57.4% (31/54)	<0.0001	0.013

1. Noninferiority by Wald's method, superiority by Fisher's Exact test
2. Symptomatic Intracranial Hemorrhage - Any PH1, PH2, RIH, SAH, or IVH associated with a decline in NIHSS ≥ 4 within 24hrs.

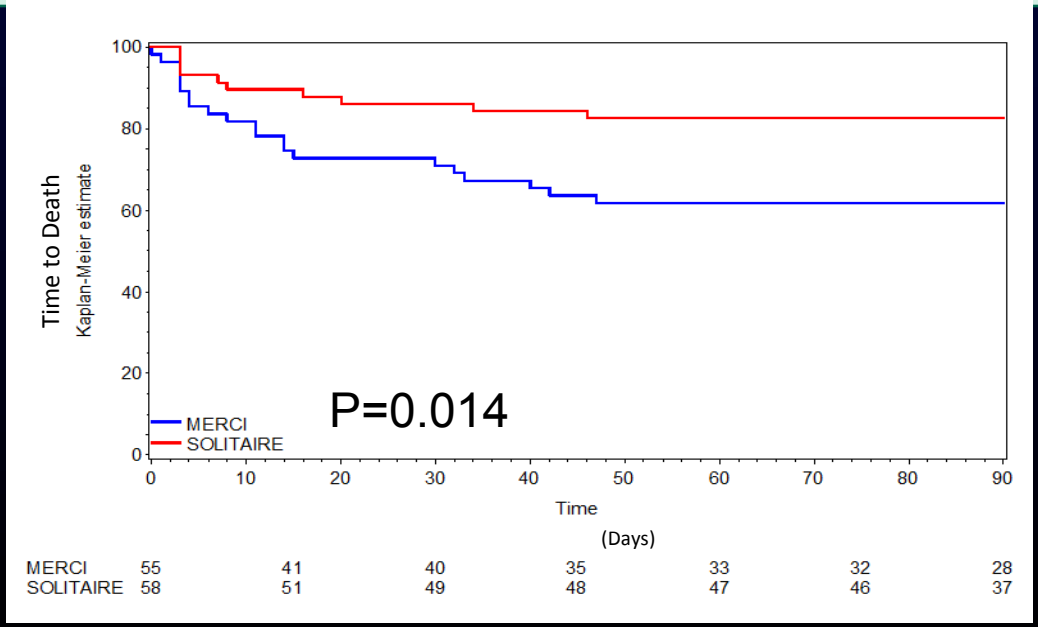
Saver J, Jahan R, Levy E, et al; SWIFT Trialists. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet.*

SWIFT IDE Clinical Trial

SWIFT Trial: Clinical Outcomes

Outcomes Among Randomized Patients	Randomized Solitaire FR N=58	Randomized Merci N=55	Non-inferiority P value[1]	Superiority P value[1]
Good neurologic outcome at 90d[2]	58.2% (32/55)	33.3% (16/48)	0.0001	0.017
Mortality at 90 days	17.2% (10/58)	38.2% (21/55)	0.0001	0.020

1. Noninferiority by Wald's method, superiority by Fisher's Exact test
2. Good neurological outcome defined as mRS ≤ 2, or equal to the prestroke mRS if the prestroke mRS was higher than 2, or NIHSS score improvement ≥ 10

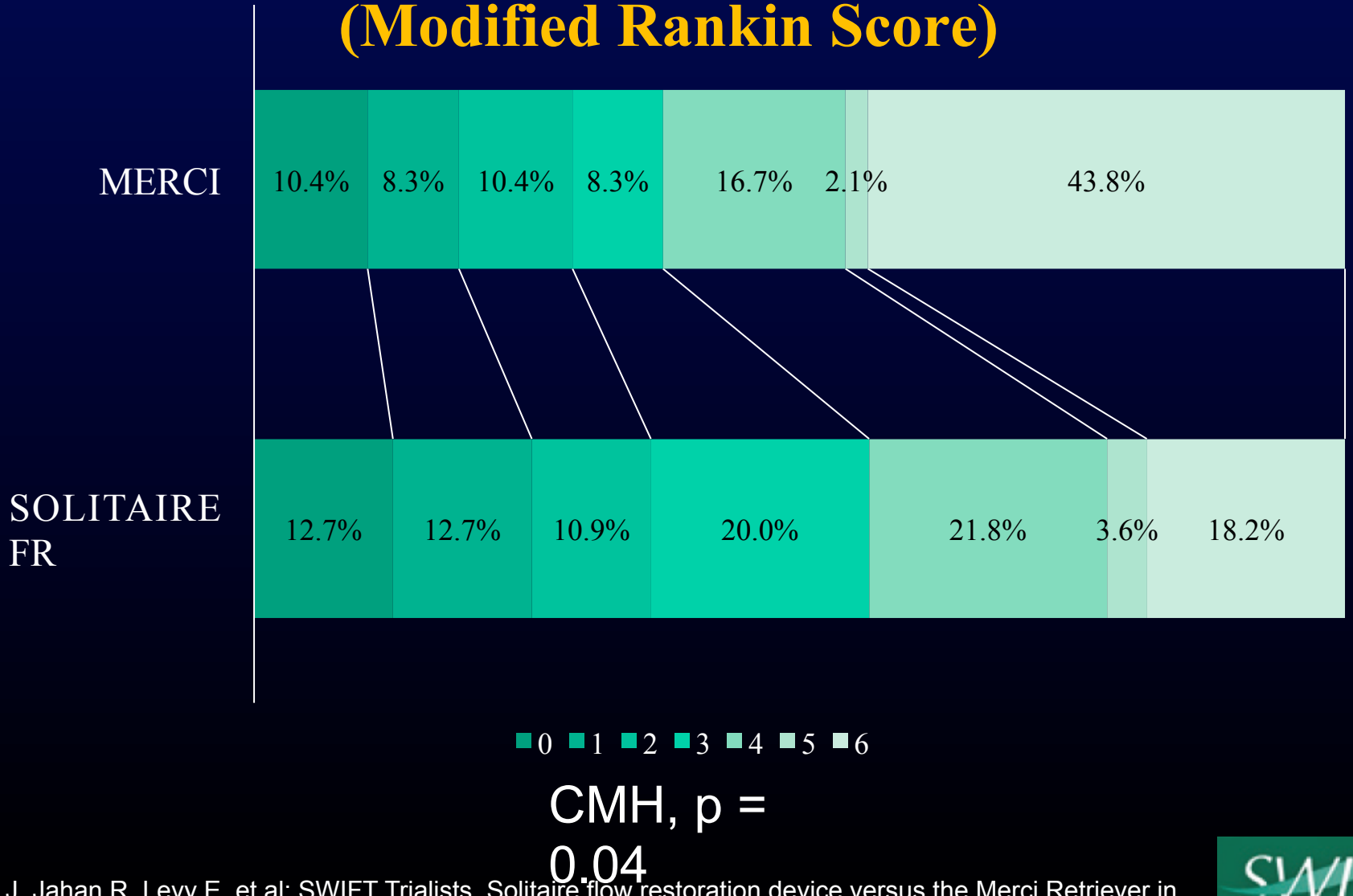


Saver J, Jahan R, Levy E, et al; SWIFT Trialists. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet.*

SWIFT IDE Clinical Trial

SWIFT Trial: Clinical Outcomes

Global Disability at 90 Days (Modified Rankin Score)



CMH, p = 0.04

Saver J, Jahan R, Levy E, et al; SWIFT Trialists. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet.*

SWIFT IDE Clinical Trial

SWIFT Trial: Hemorrhagic Outcomes

Outcomes Among Randomized Patients	Randomized Solitaire FR N=58	Randomized Merci N=55	Non-inferiority P value[1]	Superiority P value[1]
SICH	1.7% (1/58)	10.9% (6/55)	<0.0001	0.057
All ICH	17.2% (10/58)	38.2% (21/55)	0.0001	0.020

1. Fisher's Exact

Saver J, Jahan R, Levy E, et al; SWIFT Trialists. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet.*

SWIFT IDE Clinical Trial

SWIFT Trial: Adverse Events

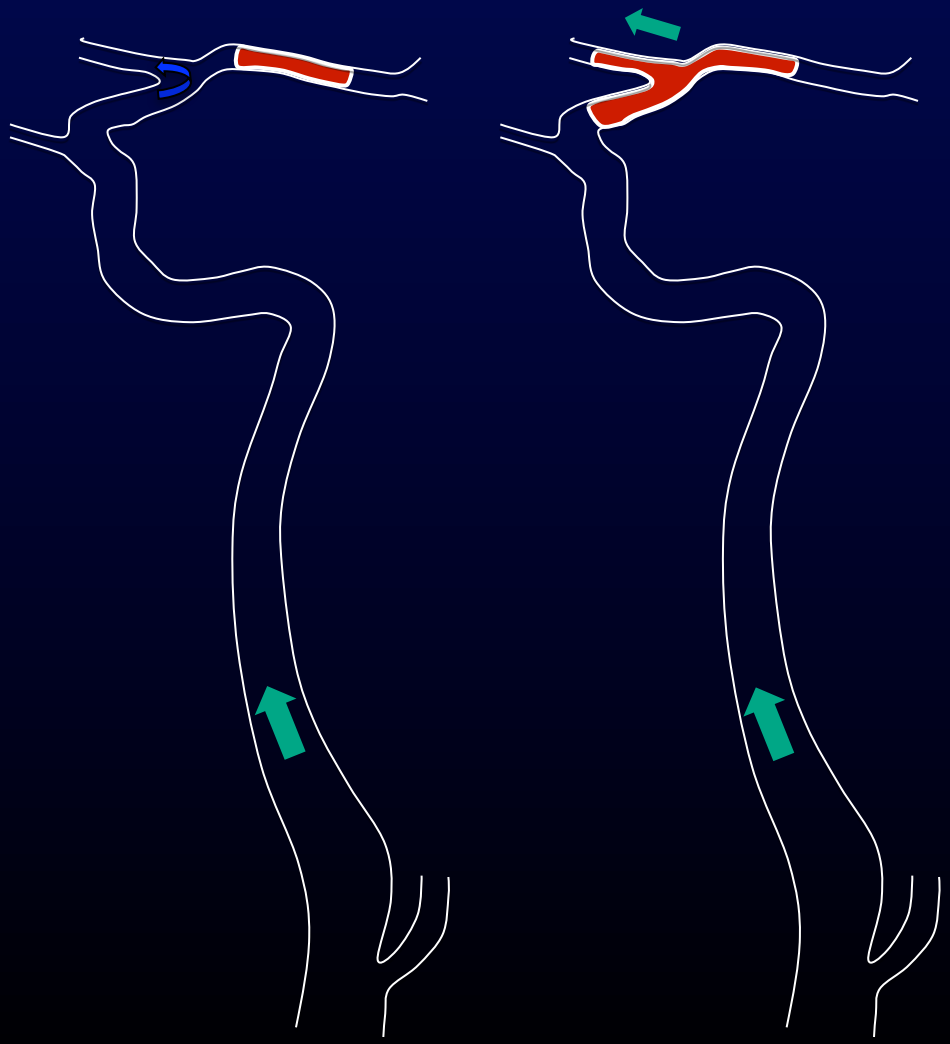
Outcomes Among Randomized Patients	Randomized Solitaire FR N=58	Randomized Merci N=55	P value[1]
All Study Device Related SAEs	8.6%	16.4%	0.26
All Procedure Related SAEs	13.8%	16.4%	0.80
Selected Adverse Events and Procedural and Technical Events			
Air Embolism	1.7% (1/58)	1.8% (1/55)	1.00
Device Fracture (Asymp ICH)	1.7% (1/58)	0.0% (0/55)	1.00
Vasospasm	13.8% (8/58)	10.9% (6/55)	0.78
Vessel Perforation	0.0% (0/58)	3.6% (2/55)	0.23
Difficulty in device delivery	3.4% (2/58)	3.6% (2/55)	1.00
Distal Emboli	3.4% (2/58)	5.5% (3/55)	0.67

1. Fisher's Exact test

Saver J, Jahan R, Levy E, et al; SWIFT Trialists. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet.*

SWIFT IDE Clinical Trial

Balloon Guide Catheter

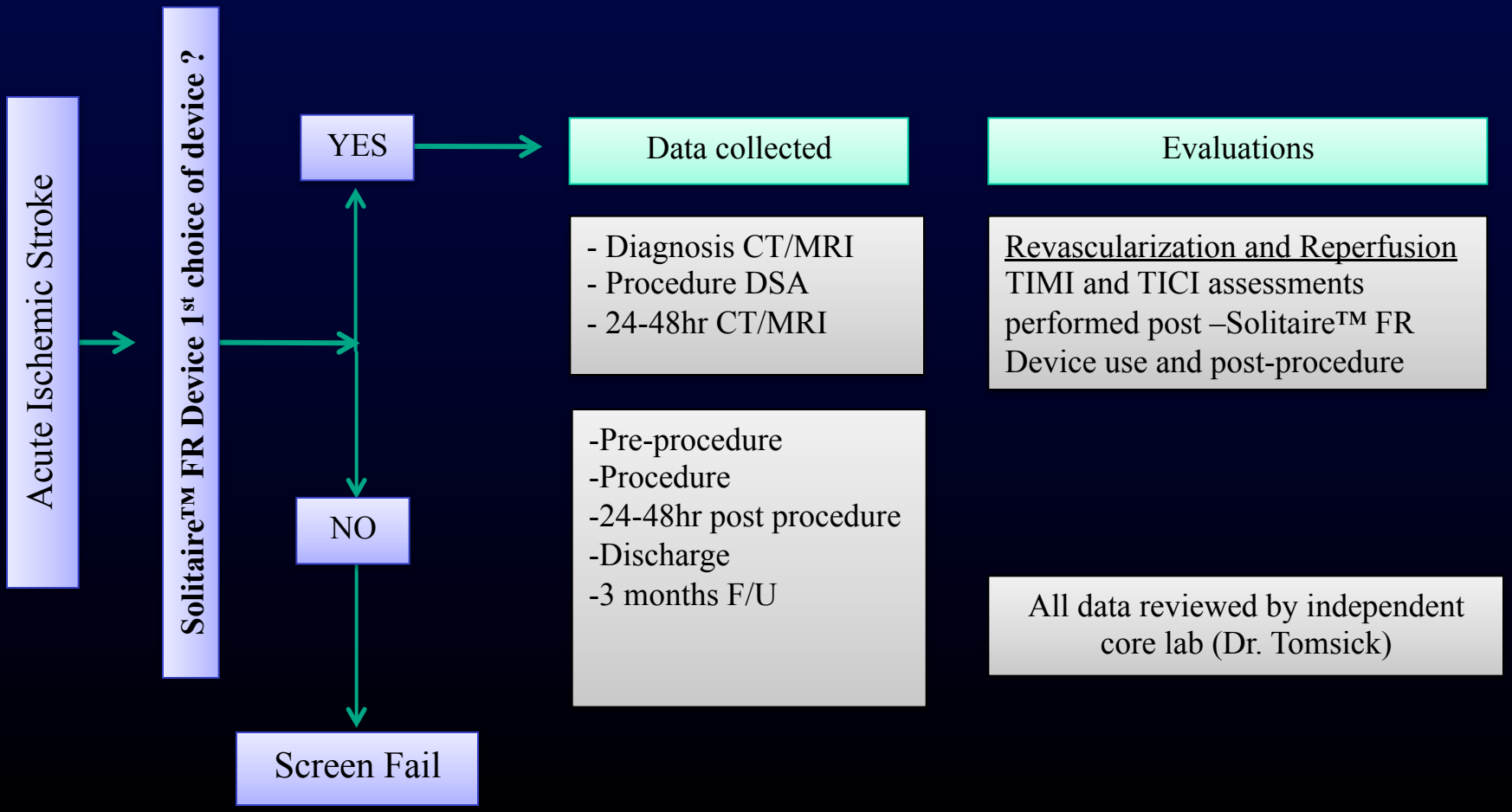


Risk of thromboembolic events

Solitaire™ FR: European Multicenter Retrospective Data

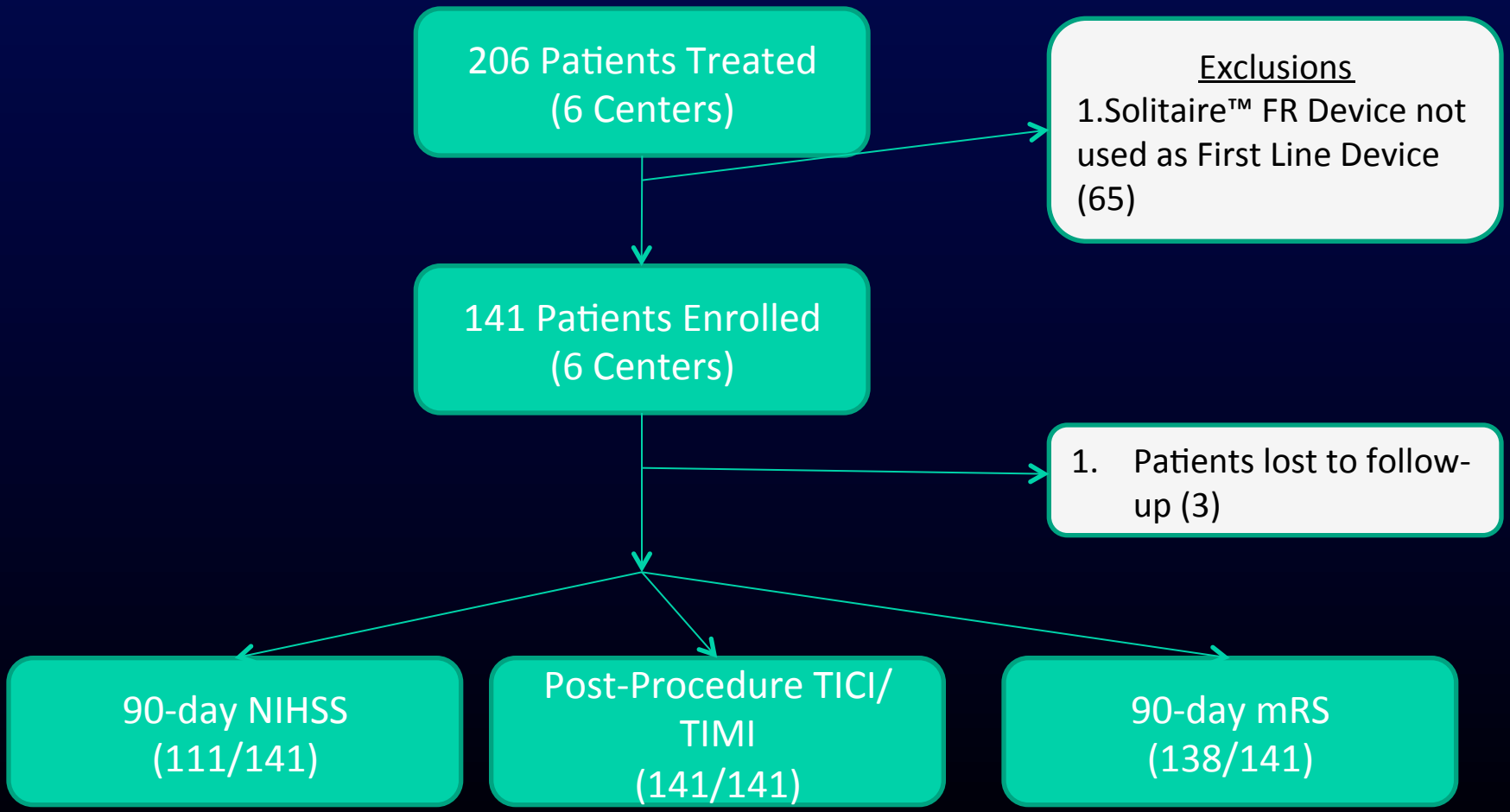
Solitaire™ FR European Retrospective Series

6 sites in EU: start of experience until July 2010



Dávalos A, Mendes Pereira V, Chapot R, et al; Retrospective Multicenter Study of Solitaire FR for Revascularization in the Treatment of Acute Ischemic Stroke. *Stroke. 2012;43:2699-2705.*

Solitaire FR European Retrospective-Subject Disposition



Dávalos A, Mendes Pereira V, Chapot R, et al; Retrospective Multicenter Study of Solitaire FR for Revascularization in the Treatment of Acute Ischemic Stroke. *Stroke. 2012;43:2699-2705.*

European Retrospective - Procedural Characteristics

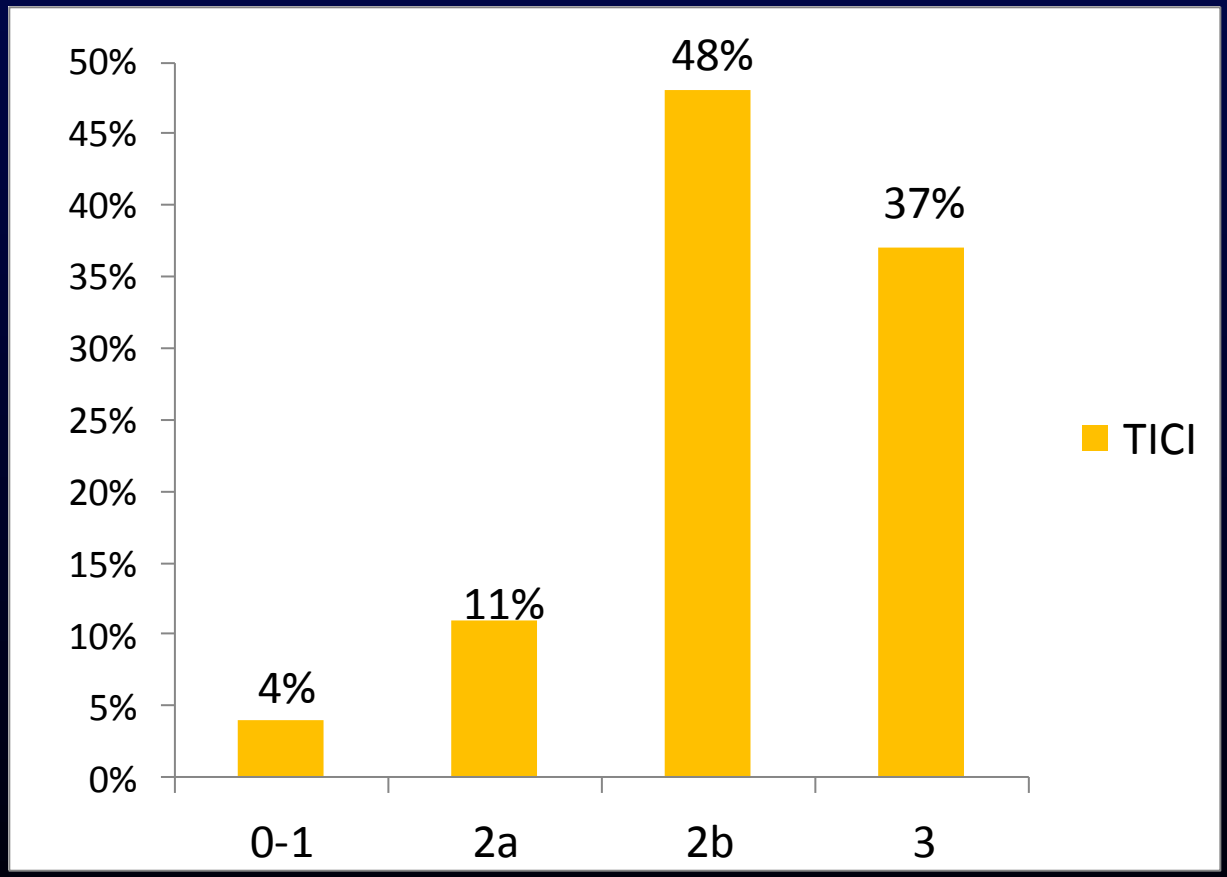
Technical Parameter	Outcome
Balloon Guide Catheter Use	74%
Technical Success	138/141 (97.8%)
Time from Groin Puncture to Revascularization - Median (min.) - Minimum - Maximum	 40 min. 14 min – 4 hr 03 min
Mean Number of Passes	1.8 (range 1-7)
Recanalization Success with ≤ 2 passes - All series (N = 141) - IV-tPA series (N= 74)	 77% 85%
Rescue Therapy Required	7 (4.9%)

Dávalos A, Mendes Pereira V, Chapot R, et al; Retrospective Multicenter Study of Solitaire FR for Revascularization in the Treatment of Acute Ischemic Stroke. *Stroke. 2012;43:2699-2705.*

European Retrospective-Revascularization Rates

Core Lab Adjudicated (T. Tomsick)

- Revascularization
  - TICI ≥ 2b: 85%
  - TIMI ≥ 2: 96%
  - AOL 3: 83%



Dávalos A, Mendes Pereira V, Chapot R, et al; Retrospective Multicenter Study of Solitaire FR for Revascularization in the Treatment of Acute Ischemic Stroke. *Stroke. 2012;43:2699-2705.*

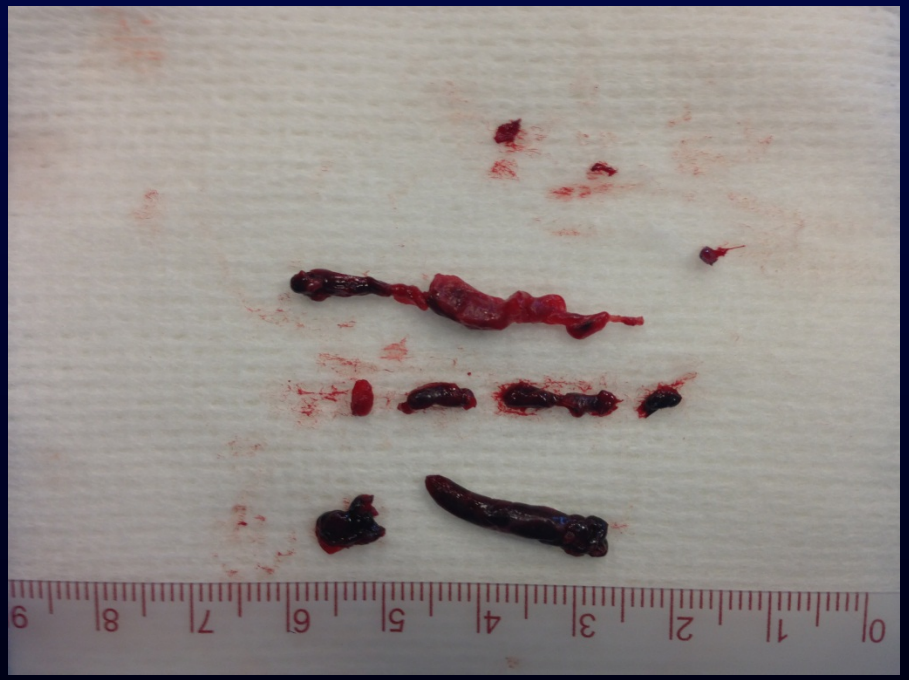
European Retrospective-Clinical Outcomes

	Overall
Clinical Outcomes (center evaluation)	Patients N=141
Good early neurologic outcome (discharge)	45(32%)
mRS≤2 at 90 days	77(55%)
Safety results	
Death at 90 days	29(21%)
Symptomatic ICH*	7(6%)
Device/Procedural related Morbidity	
Groin hematoma false aneurysm	1 (0.7%)
Arterial dissection	1 (0.7%)
Vasospasm	6/143 (4%)

*PH-1 or PH-2and Adverse Event reported or Death or increase ≥4 pts NIHSS at 24hrs

Dávalos A, Mendes Pereira V, Chapot R, et al; Retrospective Multicenter Study of Solitaire FR for Revascularization in the Treatment of Acute Ischemic Stroke. *Stroke. 2012;43:2699-2705.*

Balloon Guiding Catheter?



Dávalos A, Mendes Pereira V, Chapot R, et al; Retrospective Multicenter Study of Solitaire FR for Revascularization in the Treatment of Acute Ischemic Stroke. *Stroke. 2012;43:2699-2705.*

Recent Randomized Trials Against Medical Therapy

Endovascular vs. Medical Therapy (IV tPA)

Multivariate Predictors of Good Outcome (mRS ≤2) and Mortality at 90-Days (n=305)

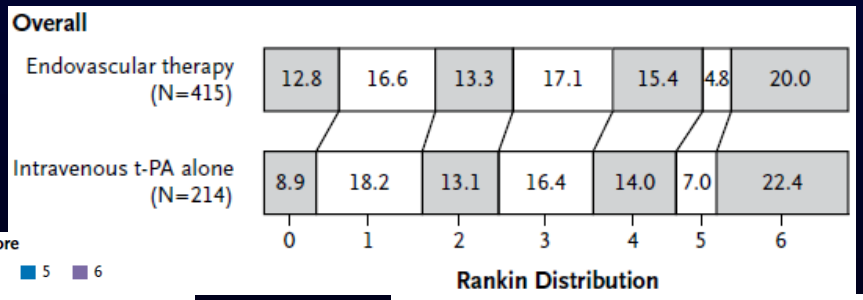
Variable	mRS 0-2		Mortality	
	Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
Revascularization	20.43 (7.74-53.92)	<0.0001	0.28 (0.16-0.50)	<0.0001
Baseline NIHSS	0.86 (0.81-0.92)	<0.0001	1.09 (1.04-1.14)	0.0001
Age, years	0.96 (0.95-0.98)	0.0004	1.05 (1.03-1.07)	<0.0001
ICA Occlusion	….	….	2.17 (1.22-3.86)	0.0084

Nogueira RG et al. Stroke, 2009

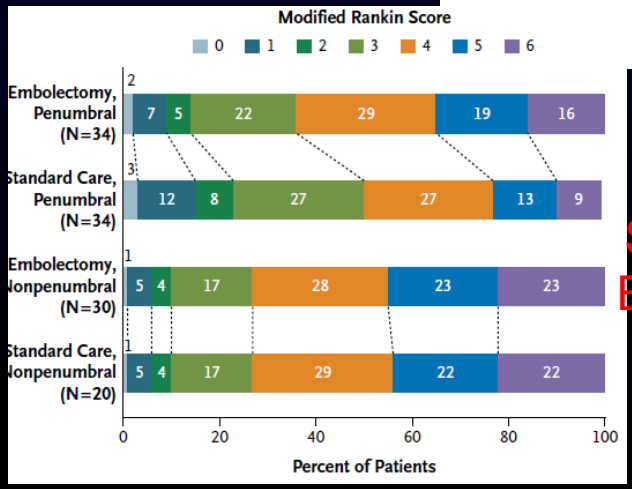
Strong correlation between recanalization and Functional Outcomes but….

Disappointing results in the recent Randomized Clinical Trials

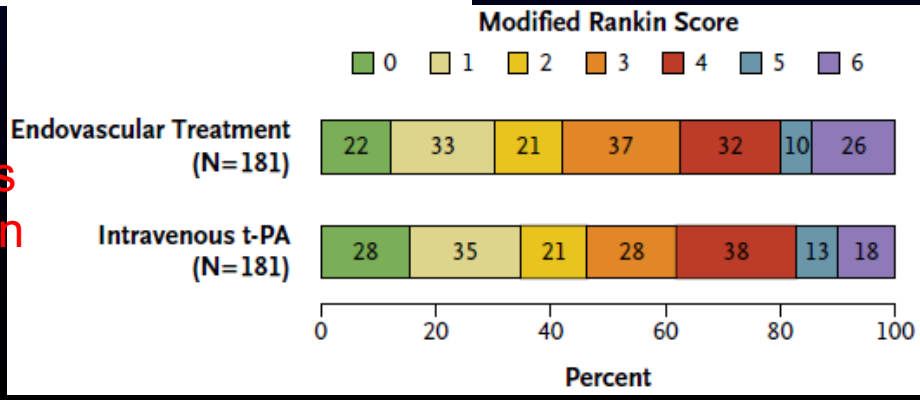
IMS III



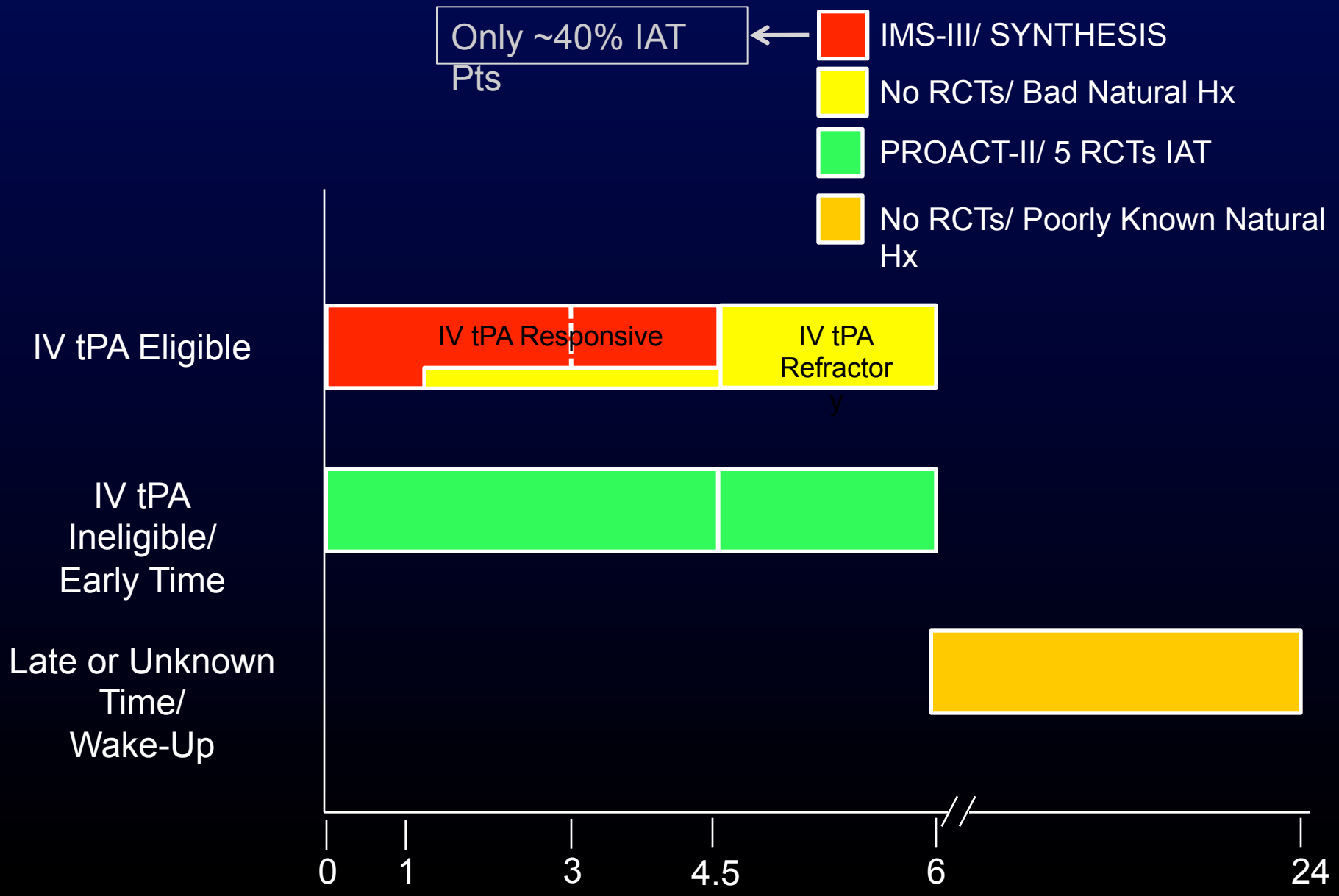
MR Rescue



Synthesis Expansion

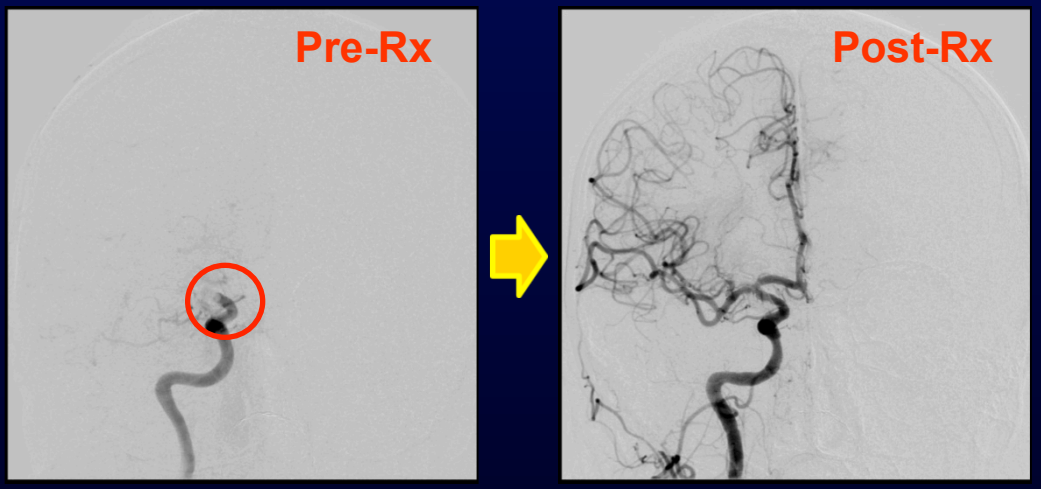


AIS LVO Patient Populations:

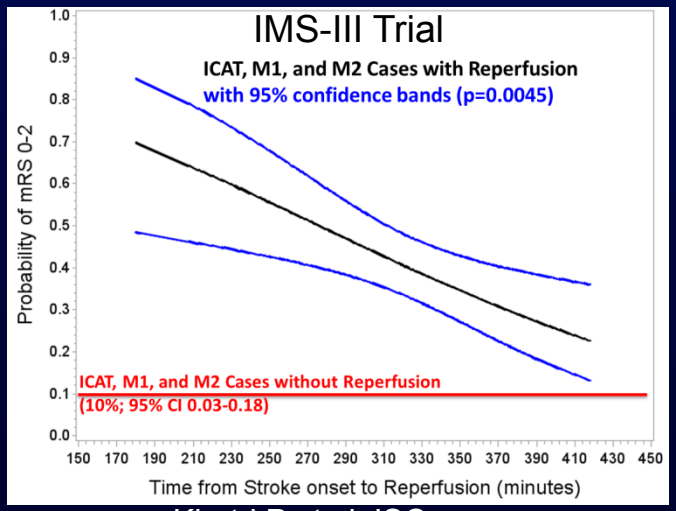


Minimal Conditions to Benefit from Endovascular Therapy

Proximal Arterial Occlusion (ICA/MCA-M1/VB)

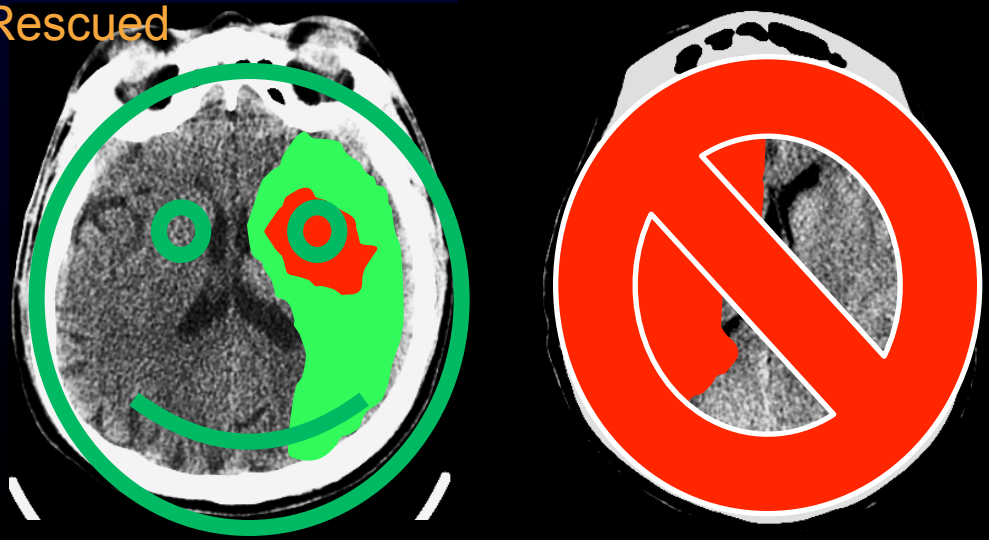


Fast Reperfusion

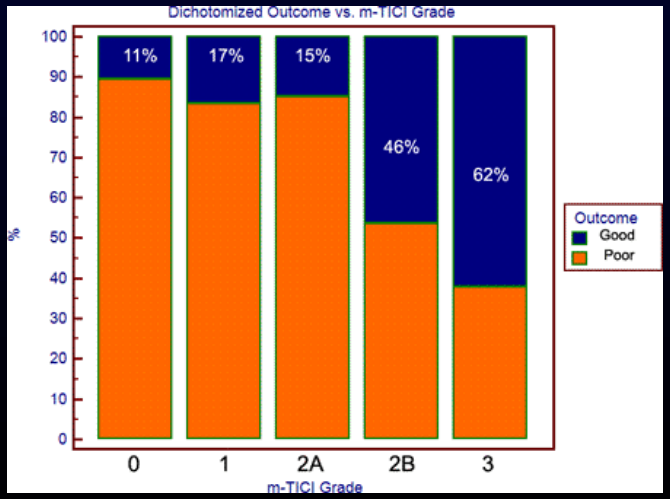


Khatri P et al. ISC, 2013

Enough Ischemic but Viable Brain that Can Be Rescued



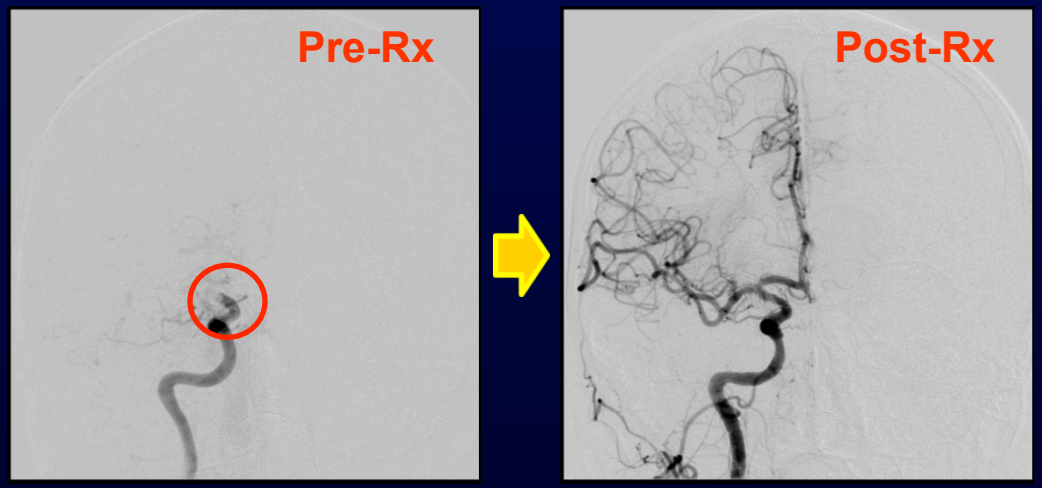
Optimal Reperfusion



Yoo AJ et al. ISC, 2013

Potential Reasons For Lack of Benefit

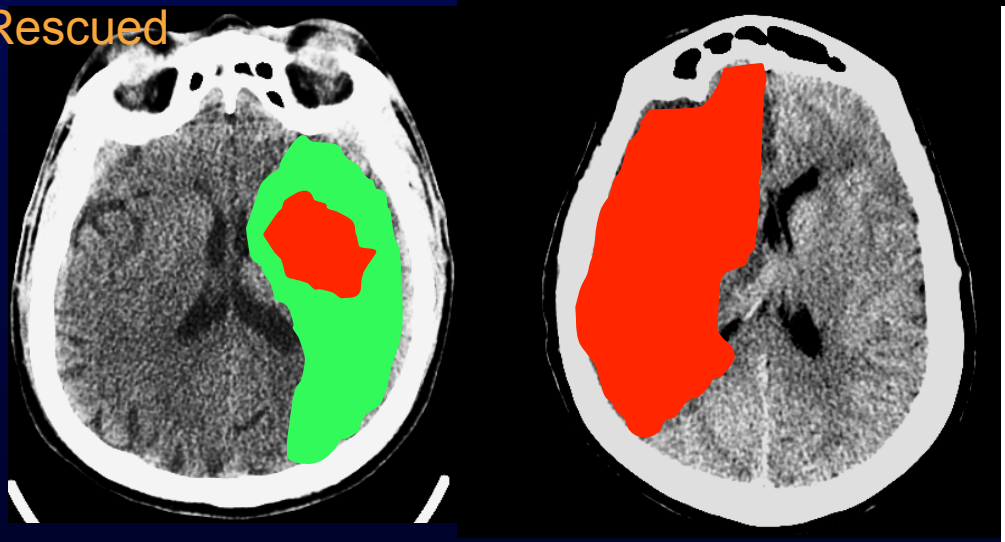
Proximal Arterial Occlusion (ICA/MCA-M1/VB)



- Lack of Target Occlusion
  - No CTA/MRA required
    - IMS-III: <1/2
    - SYNTHESIS: ~ 30%
  - Distal Occlusions = Better Responses to IV tPA + no role for IA
    - ~1/3 IMS-III distal lesions; ICA (18.9%, n=58/306), MCA-M1 (48.7%, n=149/306), or basilar (2%, n=6/306)
    - Likely more in SYNTHESIS (median bNIHSS 13)
  - IMS-III: ~1/4 Pts Randomized to IAT did not received IAT

Potential Reasons For Lack of Benefit

Enough Ischemic but Viable Brain that Can Be Rescued



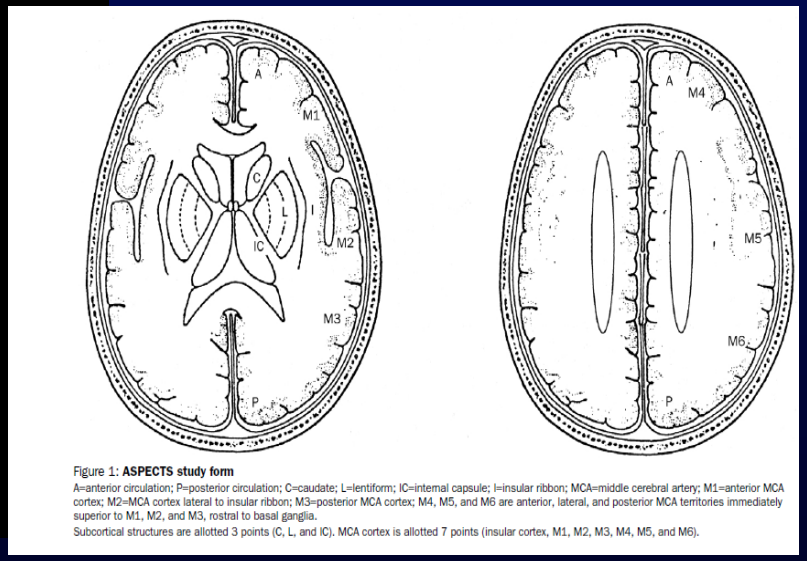


Figure 1: **ASPECTS study form**

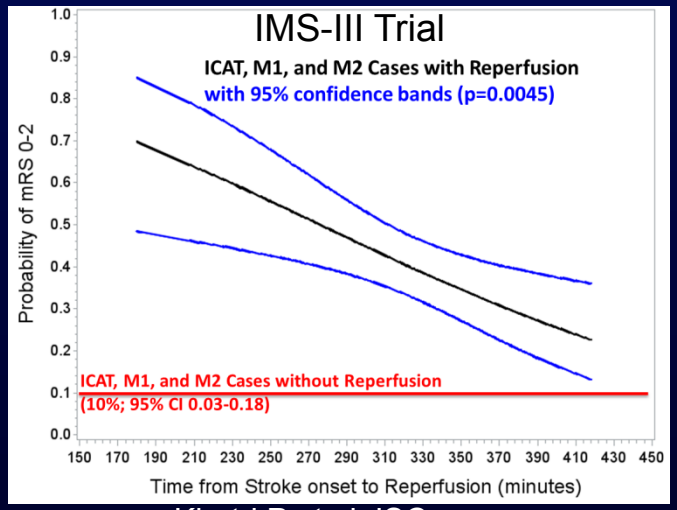
A=anterior circulation; P=posterior circulation; C=caudate; L=lentiform; IC=internal capsule; I=insular ribbon; MCA=middle cerebral artery; M1=anterior MCA cortex; M2=MCA cortex lateral to insular ribbon; M3=posterior MCA cortex; M4, M5, and M6 are anterior, lateral, and posterior MCA territories immediately superior to M1, M2, and M3, rostral to basal ganglia.

Subcortical structures are allotted 3 points (C, L, and IC). MCA cortex is allotted 7 points (insular cortex, M1, M2, M3, M4, M5, and M6).

- Lack of Target Penumbra
  - SYNTHESIS: low clinical severity - NIHSS ≤10: 36% (no benefit in PROACT-II). Like including NSTEMI…
  - IMS-III and MR Rescue: too much dead tissue prior to treatment = no independent outcomes. Like treating a STEMI with established Q waves…
    - IMS-III: ~ 1/2 pts Pre-Rx CT ASPECTS ≤7 (33% ICA; 55% M1) (no benefit in PROACT-II).
    - MR Rescue: <1/2 pts Pre-Rx infarct volume <50cc

Potential Reasons For Lack of Benefit

Fast Reperfusion

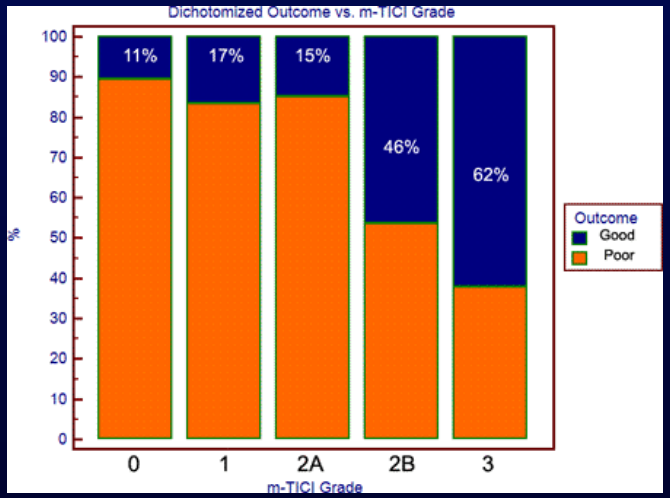


Khatri P et al. ISC, 2013

- Long Times to IA Treatment = Less Benefit from Reperfusion
  - STEMI PCI mortality benefit lost if D2B time is delayed by >1hour vs. fibrinolytic therapy door-to-needle time (Nallamothu BK. *Am J Cardiol*. 2003)
  - IMS-III: IA treatment >2-hour delay vs. IV treatment
  - SYNTHESIS: IA treatment had 1-hour delay vs. IV treatment
  - MR Rescue: mean time stroke to puncture: 6.2 h; Mean Time Imaging to puncture >2h

Potential Reasons For Lack of Benefit

Optimal Reperfusion



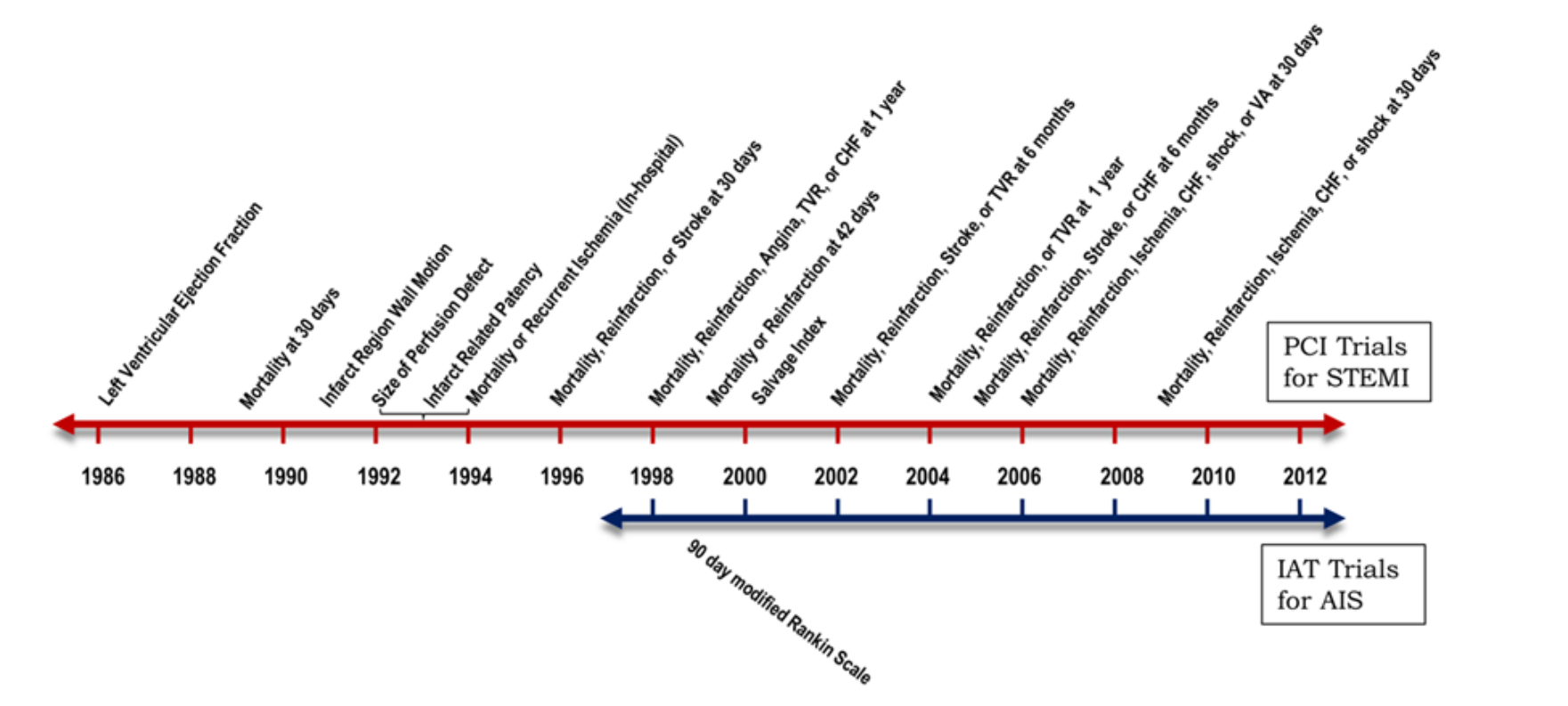
Yoo AJ et al. ISC, 2013

- Low Reperfusion Rates – Lytics and Obsolete Devices
  - IA Lytics >> 1st Generation Mechanical >>> Last Generation Mechanical
  - IA tPA only
    - ~1/2 IMS-III
    - ~2/3 SYNTHESIS
  - Obsolete device technology = Poor and Slow Reperfusion
  - TICI ≥2b Reperfusion:
    - 23-44% in IMS-III
    - 27% in MR Rescue
    - up to 85% in Stentrievers Trials

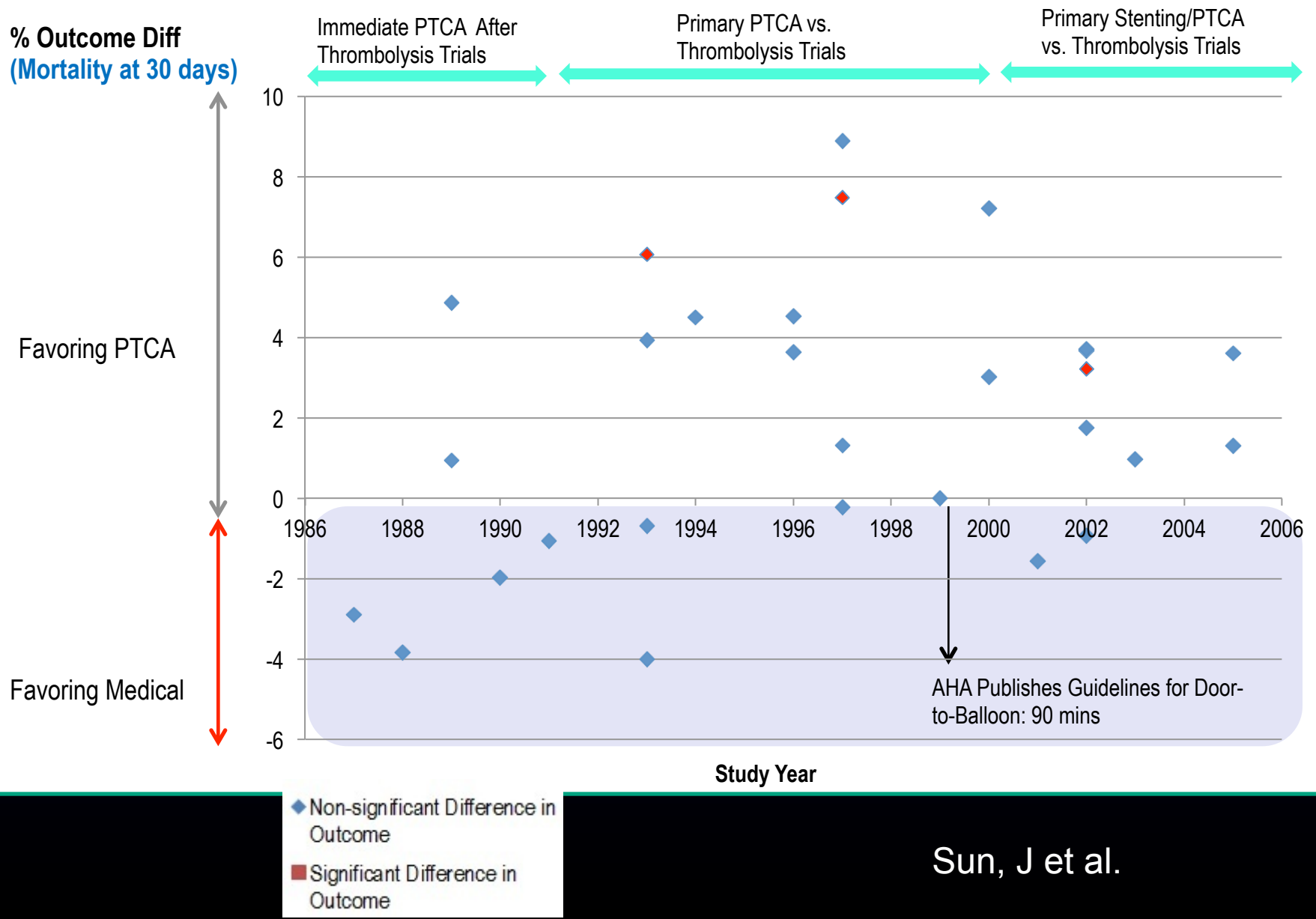
Potential Reasons For Lack of Benefit

- IV rt-PA Considerations
  - IV t-PA works
  - STEMI PCI vs. IV lysis: Short-Term Mortality NNT=45 in 23 RCTs (n-8,140) and 91in 32 observational stidues (n=185,900)(Huynh T. Circulation. 2009)
  - IA Arm = Lower tPA dosage (IMS-III)
- Lack of Equipoise = many "good"/eligible patients not enrolled
  - SYNTHESIS: 91 eligible pts not randomized because investigator's lack of equipoise
- Underpowered Studies
- Suboptimal outcome measures

Evolution of outcome measures in STEMI vs. AIS:

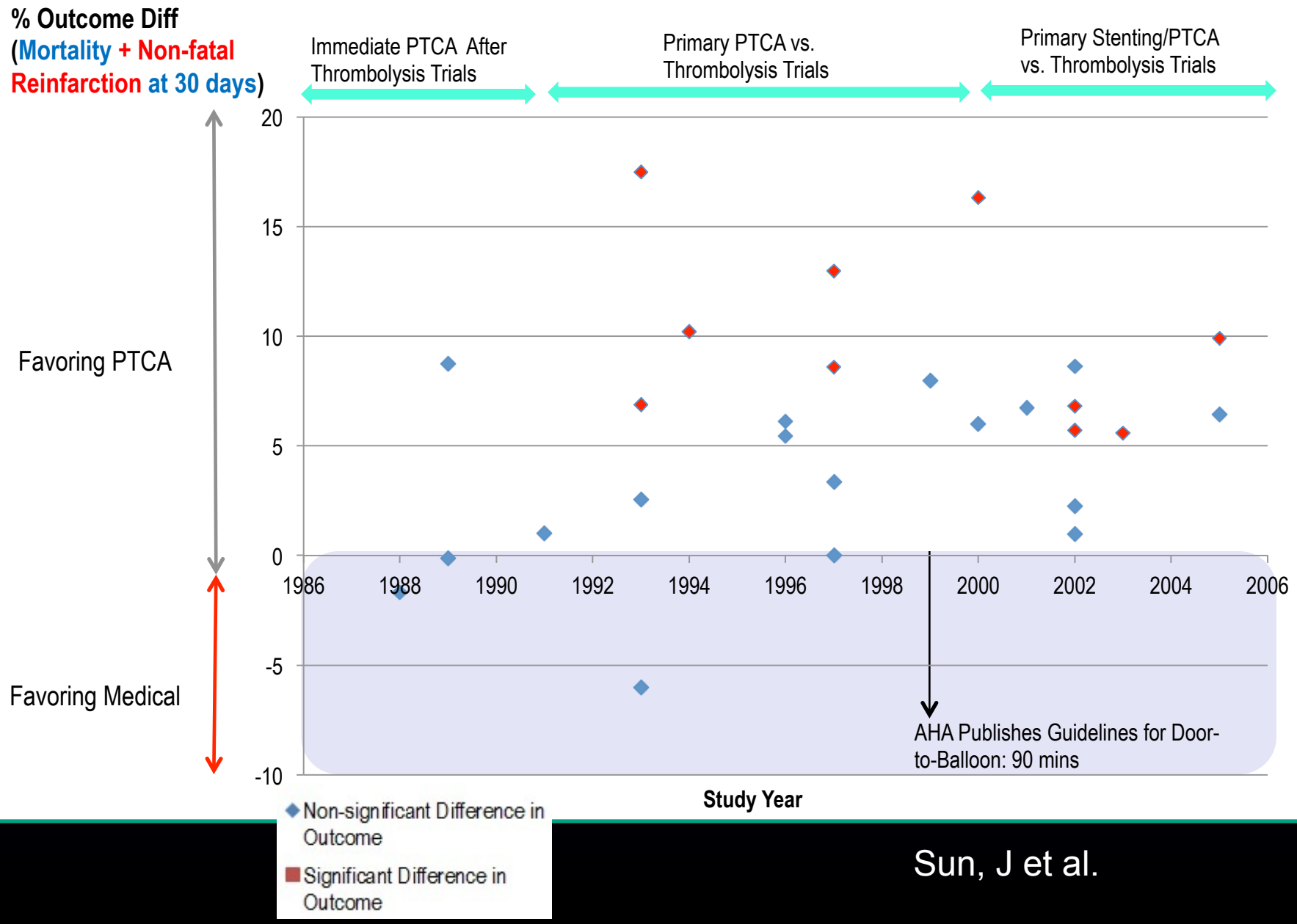


Lessons from Coronary Literature



Sun, J et al.

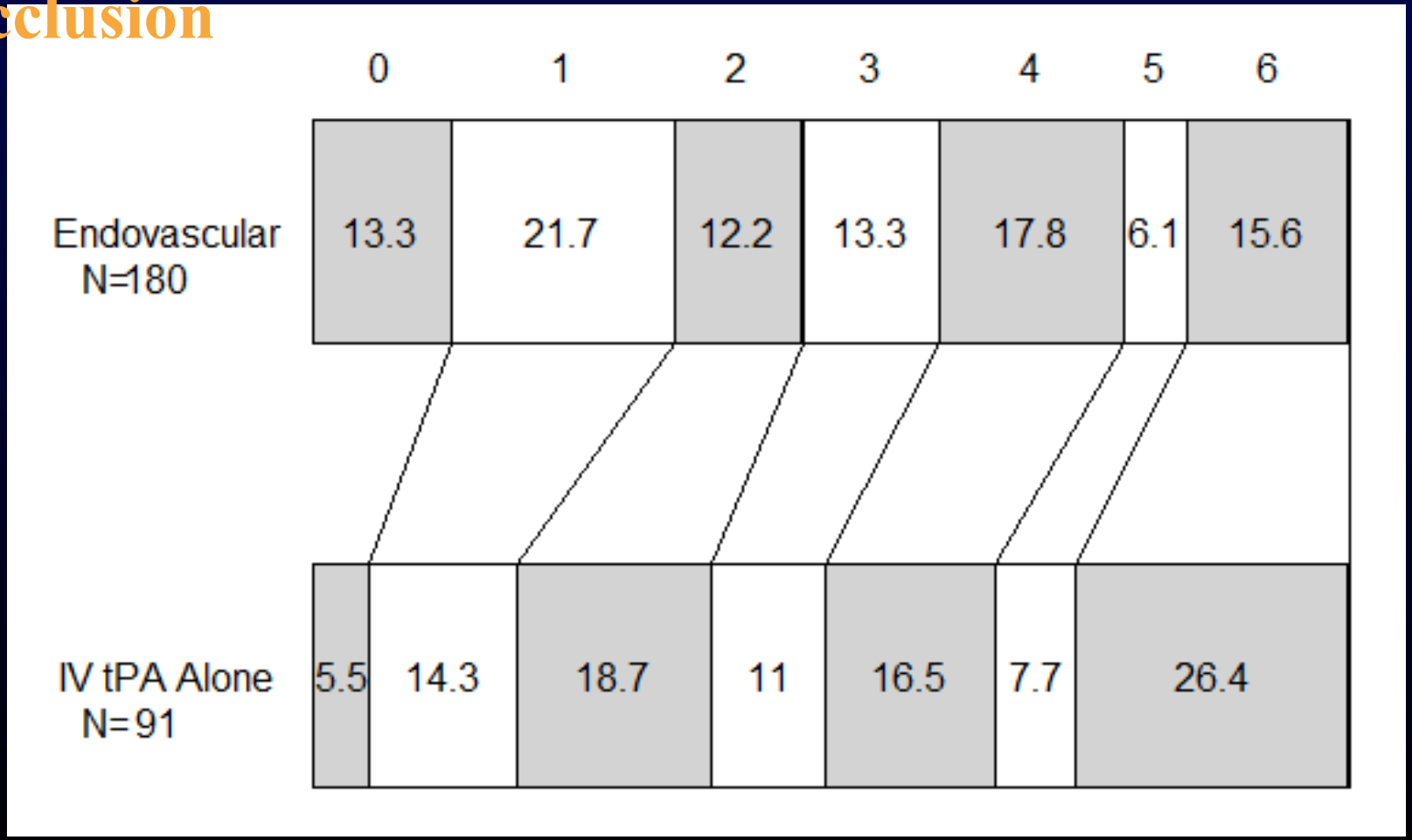
Lessons from Coronary Literature



Sun, J et al.

IMS-III: + Occlusion and Any Improvement Considered:

IMS-III: 90-Day mRS Distribution, Baseline CTA+ Occlusion



van Elteren test p-value

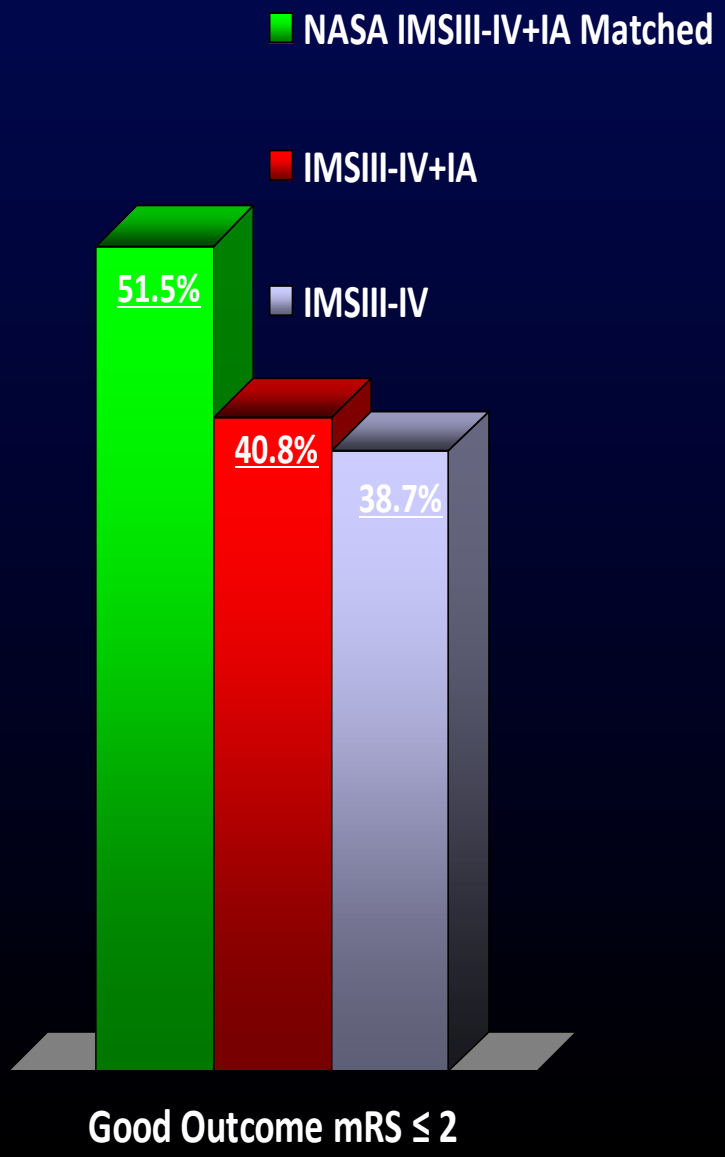
Recent Endovascular Trials = Better Outcomes!

Endpoint	Trevo2 Trevo (n=88)	Trevo2 Merci (n=90)	Trevo2 p-value (n=178)	SWIFT Solitaire (n=58)	SWIFT Merci (n=55)	SWIFT p-value (n=113)	TREVO EU (n=60)	STAR (n=202)	START (n=105)
Successful Recanalization*	86.4% (76/88) TICI ≥2a TICI 2b-3 67.8%	60.0% (54/ 90) TICI ≥2a TICI 2b-3 43.4%	< 0.0001	68.5% (37/54) TIMI 2-3 Treatable Vessels	30.2% (16/53) TIMI 2-3 Treatable Vessels	< 0.0001	90.0% TICI ≥2a	84.2% (160/190) TICI ≥2b	85% TIMI 2-3
90-Day mRS 0-2: 40-58%									
mRS ≥ 2, OR ↓NIHSS ≥ 10 points, OR return to baseline mRS at 90 days	52.9% (45/85)	42.5% (37/87)	0.2218	58.2% (32/55)	33.3% (16/48)	0.0172	72.0%	N/A	N/A
90-Day mRS 6: 7-33%									
mRS 0-3 at 90d	49.4% (42/85)	37.9% (33/87)	0.1663	56.4% (31/55)	37.4% (18/48)	0.0752	N/A	74%	N/A
sICH: 1.5-6.8%							5.0%		

Nogueira RG et al. Lancet, Aug 2012; Saver J et al. Lancet, Aug 2012;
Wahlgren N , ISC 2012, Pereira VM, ISC 2013; Frei D et al. ISC 2013

IMS3-Like Subgroup Analysis of the North American Solitaire Acute Stroke Registry

- **354** patients were enrolled in NASA
- **156** NIMG vs. **434** IMS-III IV+IA (mainly IA tPA/Merci; <0.1% Stentriever) vs. **222** IMS-III IV tPA
- Baseline variables were not different (NIHSS was higher in NIMG 19 vs 17 in IMS-III IV+IA and 18 in IMS-III IV).
- Good outcome: NIMG **51.5%** vs. 40.8% in IMS-III IV+IA and 38.7% in IMS-III IV
- Mortality: NIMG 24.6% vs. 19.1% in IMS-III IV+IA and 21.6% in IMS-III IV.
- mTICI 2b-3: NIMG **70%**; vs 40% in IMS-III IV+IA .
- mTICI 3: NIMG **41%** vs 2% in IMS-III IV +IA.



Zaidat OO, Nogueira RG et al AAN 2013

Smaller Final Infarct Volumes with Intra-Arterial vs. Intravenous vs. Medical Therapy Alone

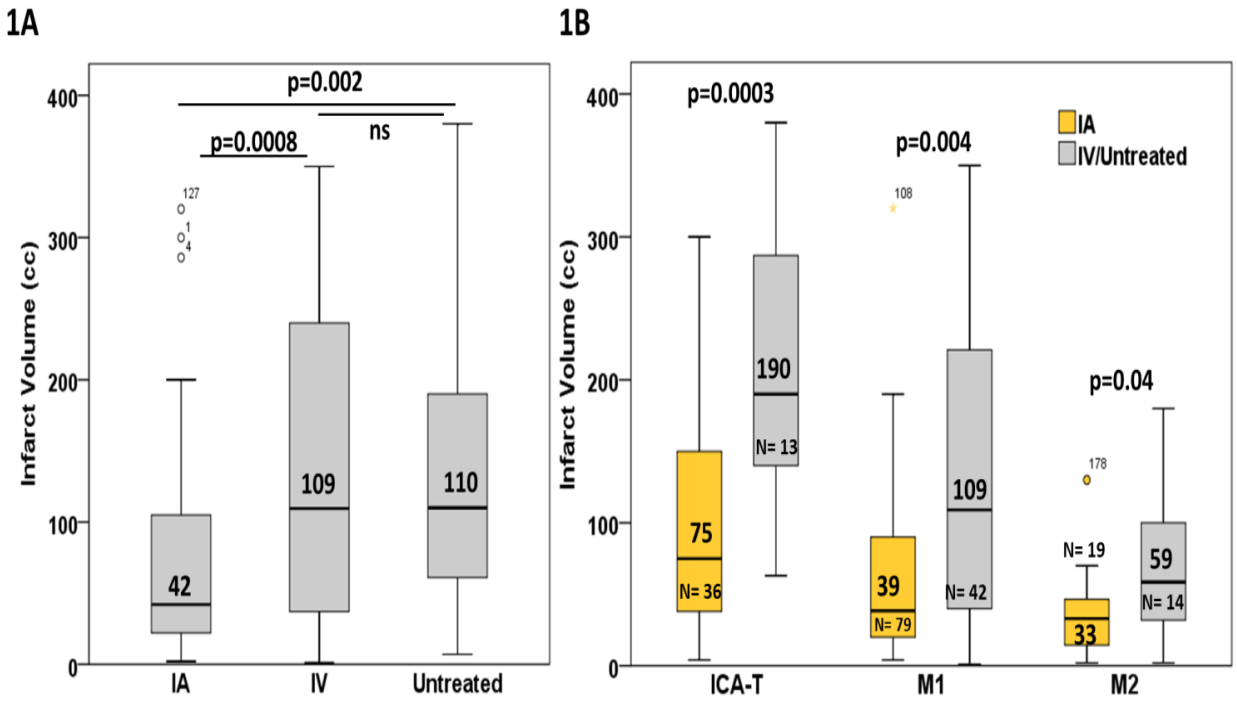
- 203 AIS pts; ICA-T, MCA-M1 or M2; CT within 6h TLSW
- Age, 65.9±15.7 yrs; median bNIHSS 19 [IQR, 14-23]
- No difference in age, bNIHSS, occlusion site. Time to CT shorter in IVT
- IAT (n=134; [67.9% IV tPA), IVT (n=38), and NRT (n=31)
- IAT: Penumbra (62.7%; n= 84), Merci (41.8%; n=56), Stentrievers (13.4%; n=18)
- Infarct volumes-IAT (42 cm3) vs. IVT (109 cm3; *P*=.001) vs. NRT group (110 cm3; *P*.01)
- IAT smaller infarct

ORIGINAL CONTRIBUTION

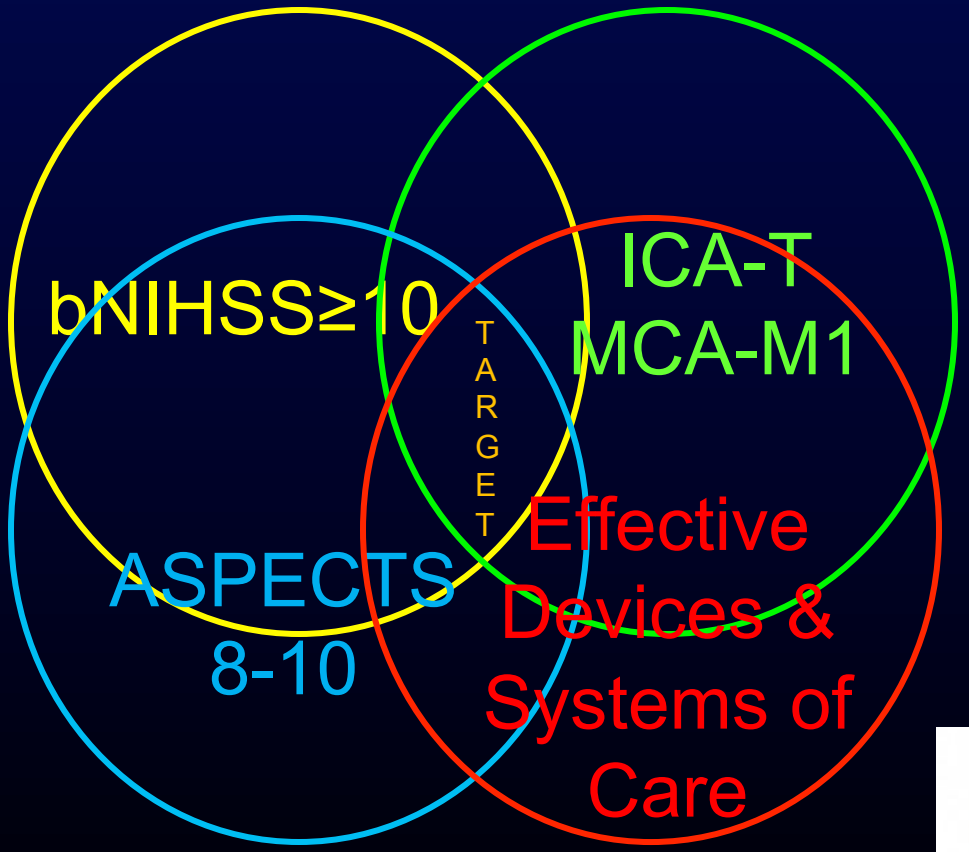
ONLINE FIRST

Comparison of Final Infarct Volumes in Patients Who Received Endovascular Therapy or Intravenous Thrombolysis for Acute Intracranial Large-Vessel Occlusions

Srikant Rangaraju, MD; Kumiko Owada, MD; Ali Reza Noorian, MD; Raul G. Nogueira, MD; Fadi Nahab, MD; Brenda A. Glenn, RN, BSN, ACNP; Samir R. Belagaje, MD; Aaron M. Anderson, MD; Michael R. Frankel, MD; Rishi Gupta, MD



Recent Trials – Lessons Learned



Designing Success:

Problem	Solution
Highly effective device	Stent Retrievers or Penumbra Max System
Clots to attack	CTA/MRA
Clots poorly responsive to IVT	ICA/M1
Brain to save/Penumbra	Clinical Core Mismatch of Perfusion Imaging
Patients who will respond	Randomize ALL eligible
Minimize progression	Door to puncture optimization
Concomitant therapy	Full dose TPA if eligible
Patient Volume	Need to Collaborate!

SWIFT PRIME

SWIFT Prime: Study Design

Study Overview	
Design	Global, multi-center, prospective, randomized, open, blinded endpoint (PROBE) IDE Study
Purpose	This study is to determine if patients experiencing an Acute Ischemic Stroke due to large vessel occlusion, treated with combined IV t-PA and Solitaire™ FR device within 6 hours of symptom onset have less stroke-related disability than those patients treated with IV t-PA alone.
Population	• Acute ischemic stroke with large vessel occlusion (ICA, MCA – M1, carotid terminus) • Able to be treated with SOLITAIRE™ FR device within 6 hours of stroke onset • Has received or is able to be treated with IV t-PA within 4.5 hours post stroke onset • Established penumbral mismatch (patient selection by RAPID)

SWIFT Prime: Study Objectives

Study Endpoints	
Primary	90-day global disability assessed via the blinded evaluation of modified Rankin Score (mRS)
Secondary: Clinical	• Death due to any cause at 90 days • Functional independence as defined by modified Rankin Scale (mRS) score $\leq$ 2 at 90 days • Change in NIH Stroke Scale score at 27 ±3hrs post randomization
Sites	Up to 60 centers total (40 US)
Sample Size	833
Follow-up	Follow-up: 27 ±3 hours, 7-10 Days/Discharge, 30 Days, 90 Days