



ESCAPE

Endovascular treatment for **S**mall **C**ore and **A**nterior circulation
Proximal occlusion with **E**mphasis on minimizing CT to
recanalization times

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on behalf of the ESCAPE Trial Investigators



Disclosures

The official trial sponsor was the “Governors of the University of Calgary” with grants from a consortium:

- Covidien (now Medtronic)
- University of Calgary
- Alberta Health Services
- Heart & Stroke Foundation Canada
- Alberta Innovates Health Solutions

The trial was registered: NCT 01778335

History & Background

“Standing on the shoulders of giants”

- Sussmann (1958), Zeumer (1990), del Zoppo (1992)
- PROACT-2 (1999) – Furlan et al.
- EMS (1999) – Lewandowski et al.
- IMS1, 2 (2004, 2007) – Broderick et al.
- IMS3 (2013) -Broderick et al.
- MR-RESCUE (2013) - Kidwell et al.
- SYNTHESIS-Expansion (2013) - Ciccone et al.
- MR CLEAN (2015) – Berkhemer et al.

2013: Neutral Trials

ORIGINAL ARTICLE

ORIGINAL ARTICLE

Endovascular Therapy after Intravenous t-PA versus t-PA Alone for Stroke

Joseph P. Broderick, M.D., Yuko Y. Palesch, Ph.D., Andrew M. Demchuk, M.D., Sharon D. Yeatts, Ph.D., Pooja Khatri, M.D., Michael D. Hill, M.D., Edward C. Jauch, M.D., Tudor G. Jovin, M.D., Bernard Yan, M.D., Frank L. Silver, M.D., Rüdiger von Kummer, M.D., Carlos A. Molina, M.D., Bart M. Demaerschalk, M.D., Ronald Budzik, M.D., Wayne M. Clark, M.D., Osama O. Zaidat, M.D., Tim W. Malisch, M.D., Mayank Goyal, M.D., Wouter J. Schonewille, M.D., Mikael Mazighi, M.D., Ph.D., Stefan T. Engelter, M.D., Craig Anderson, M.D., Ph.D., Judith Spilker, R.N., B.S.N., Janice Carrozzella, R.N., B.A., R.T.(R.), Karla J. Ryckborst, R.N., B.N., L. Scott Janis, Ph.D., Renée H. Martin, Ph.D., Lydia D. Foster, M.S., and Thomas A. Tomsick, M.D., for the Interventional Management of Stroke (IMS) III Investigators

A Trial of Imaging Selection and Endovascular Treatment for Ischemic Stroke

Chelsea S. Kidwell, M.D., Reza Jahan, M.D., Jeffrey Gornbein, Dr.P.H., Jeffrey R. Alger, Ph.D., Val Nenov, Ph.D., Zahra Ajani, M.D., Lei Feng, M.D., Ph.D., Brett C. Meyer, M.D., Scott Olson, M.D., Lee H. Schwamm, M.D., Albert J. Yoo, M.D., Randolph S. Marshall, M.D., Philip M. Meyers, M.D., Dileep R. Yavagal, M.D., Max Wintermark, M.D., Judy Guzy, R.N., Sidney Starkman, M.D., and Jeffrey L. Saver, M.D., for the MR RESCUE Investigators*

ORIGINAL ARTICLE

Endovascular Treatment for Acute Ischemic Stroke

Alfonso Ciccone, M.D., Luca Valvassori, M.D., Michele Nichelatti, Ph.D., Annalisa Sgoifo, Psy.D., Michela Ponzio, Ph.D., Roberto Sterzi, M.D., and Edoardo Boccardi, M.D., for the SYNTHESIS Expansion Investigators*

Speed

1. Immediate vascular imaging (CT and CTA) is going to be the standard for all stroke
2. We have to act quickly and decisively. We need to “feel the need for speed”. Time is brain.



ESCAPE Conception

Question: “Do I take this patient for endovascular treatment (thrombectomy)?”

1. Sequential patient randomization
2. Fast and simple imaging paradigm
3. Quick workflow – parallel processing
4. Effective technology & technique to get TICI 2b/3 reperfusion

Necessity is the mother of invention

What we set out to solve in 2012...

Problem: rapid secular change in stroke care with novel technology; trials take too long to get done; cherry picking

Solution: rapid, sequential patient enrolment

Problem: failure to exclude patients with large core

Solution: insist on use of ASPECTS to exclude large core; personally check scan quality at sites; further prevent mistakes by correlating with collateral score

Problem: interventional treatment requires definition of a target lesion

Solution: CTA to identify proximal occlusion

Necessity is the mother of invention

What we set out to solve in 2012...

Problem: Absent collaterals means a very fast trajectory to infarction

Solution: Exclude patients with absent collaterals on mCTA

Problem: Treatment is too slow. Drip 'n ship cases.

Solution: Aggressive time targets. Use the imaging → reperfusion time, thereby allowing drip 'n ship cases

Problem: Incomplete reperfusion

Solution: modern retrievable stent technology and target TIMI 2b/3 flow (complete or near complete reperfusion)

Methods

- 22 centres in Canada (11), US (6), Korea (3), UK (1), Ireland (1)
- Acute ischemic stroke patients within a 12-hour window from onset, good functional status, with no age limit
- tPA given when patient eligible (no waiting for tPA response)
- Imaging must have shown: small core, proximal intracranial artery occlusion, moderate-good collaterals using CT, mCTA (use of MRI discouraged)
- Intensive quality improvement program with personalized site visits

Inclusion and exclusion criteria

- > 5 NIHSS
- < 12 hours from symptom onset
- Adult; No age limit
- Good pre-morbid status

- CT head: ASPECTS > 5 (exclude large core)
- CTA: ICA + M1 or M1 or functional M1 (all M2s)
- CTA (preferably multiphase): moderate to good collaterals

ESCAPE – Methods Paper Int J Stroke 2015

Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times

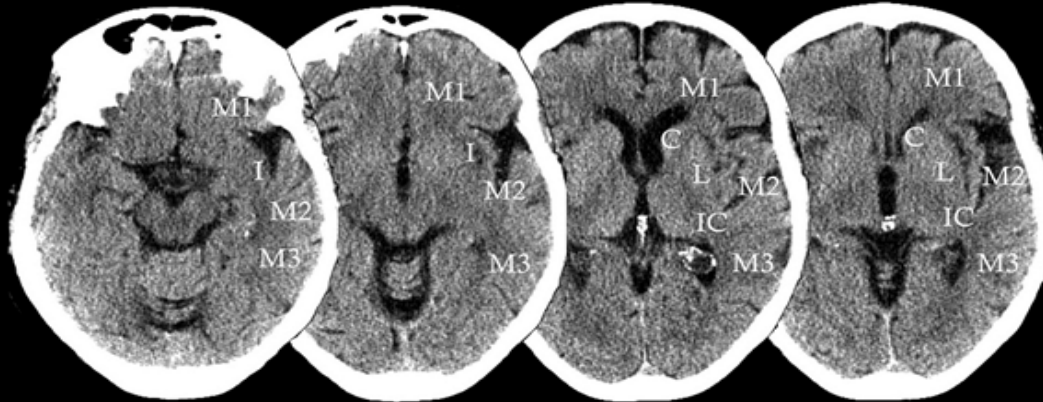
Protocol

Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times (ESCAPE) trial: methodology

Andrew M. Demchuk^{1,2,3}, Mayank Goyal^{1,2}, Bijoy K. Menon^{1,3}, Muneer Eesa^{1,2}, Karla J. Ryckborst¹, Noreen Kamal^{1,3}, Shivanand Patil², Sachin Mishra⁴, Mohammed Almekhlafi^{1,2,5}, Privia A. Randhawa¹, Daniel Roy⁶, Robert Willinsky⁷, Walter Montanera⁸, Frank L. Silver⁹, Ashfaq Shuaib¹⁰, Jeremy Rempel¹¹, Tudor Jovin¹², Donald Frei¹³, Biggya Sapkota¹⁴, J. Michael Thornton¹⁵, Alexandre Poppe⁶, Donatella Tampieri¹⁶, Cheemun Lum¹⁷, Alain Weill⁶, Tolulope T. Sajobi^{1,3,18}, and Michael D. Hill^{1,2,3,18,19*} for the ESCAPE Trial Investigators[†]

Imaging - ASPECTS

Ganglionic Level



Examine all the images at the ganglionic and supra-ganglionic levels.

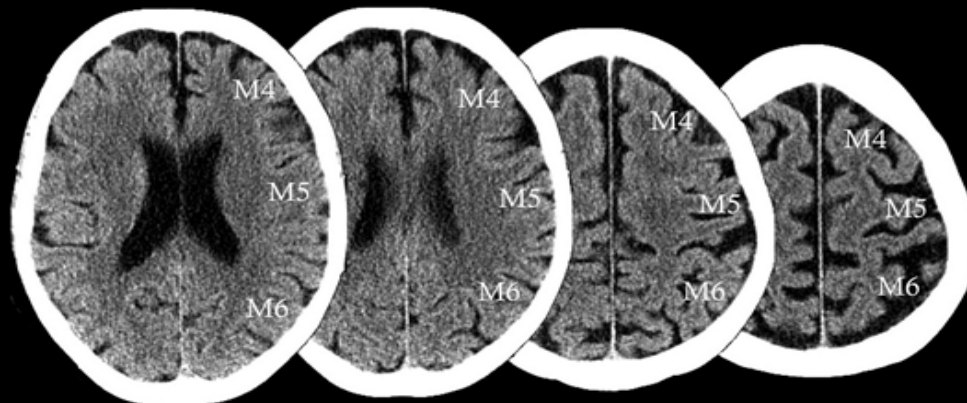
Take off 1 pt from 10 for every region that is affected

ASPECTS

8-10 Small core.

6-7 Moderate core.

0-5 Large core.



Supraganglionic Level

ASPECTS = 10 (Eligible for ESCAPE)



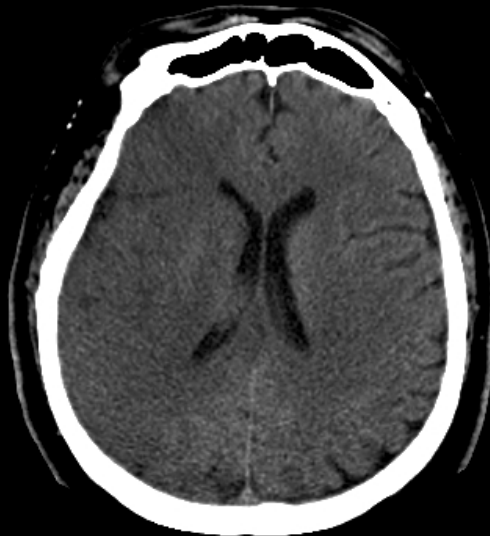
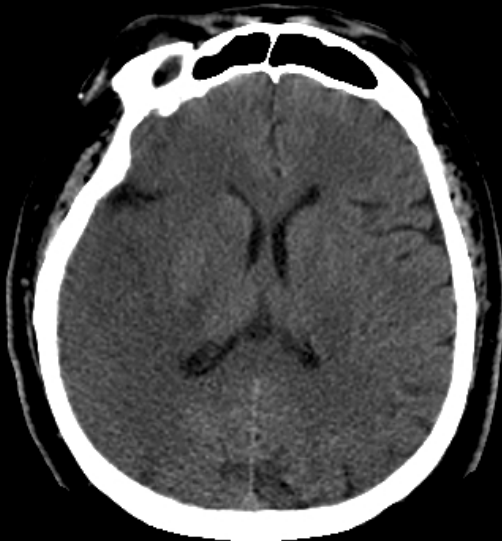
L Hemisphere



ASPECTS = 0 (NOT Eligible for ESCAPE)



R hemisphere



aspectsinstroke.com

Understanding Alberta Stroke Program Early CT Score (ASPECTS)



FACULTY OF MEDICINE | UNIVERSITY OF CALGARY

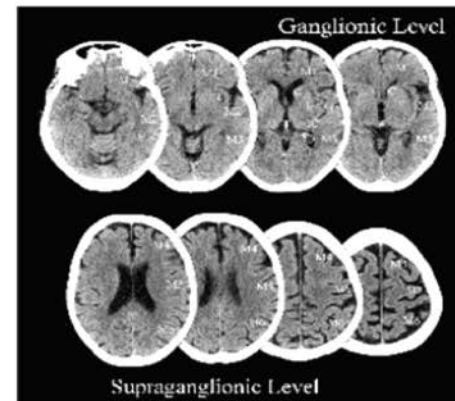
[Home](#) [Imaging in Acute Stroke](#) [ASPECTS](#) [Scan Parameters](#) [Training for ASPECTS](#) [Trial](#) [Contacts](#)

Alberta Stroke Program Early CT score (ASPECTS) is a 10-point quantitative topographic CT scan score

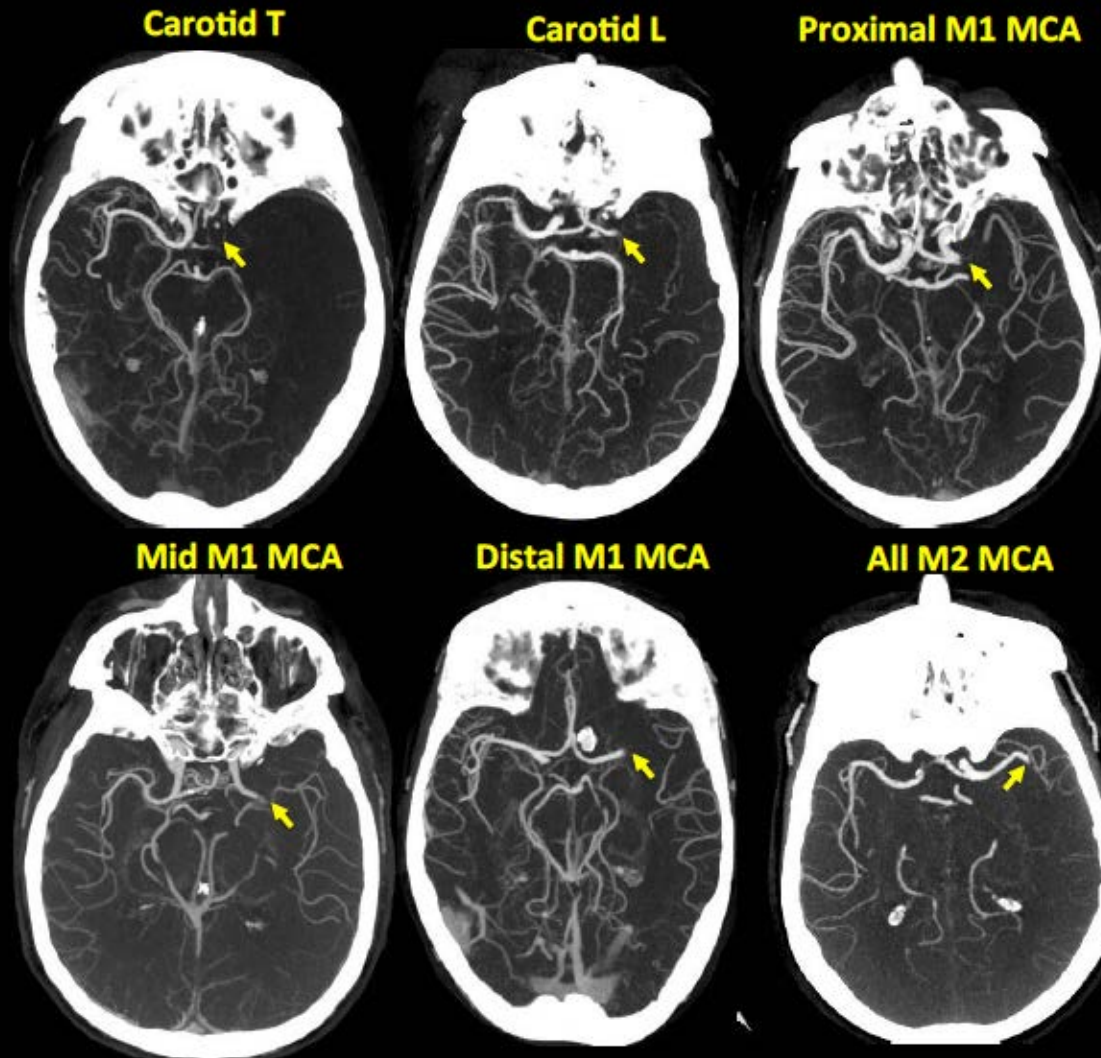
ASPECTS was developed to offer the reliability and utility of a standard CT examination with a reproducible grading system to assess early ischemic changes on pretreatment CT studies in patients with acute ischemic stroke of the anterior circulation

ASPECTS CT score is simple and reliable

We describe the use of ASPECTS in detecting early ischemic signs on NCCT brain scan



Imaging – CTA occlusion

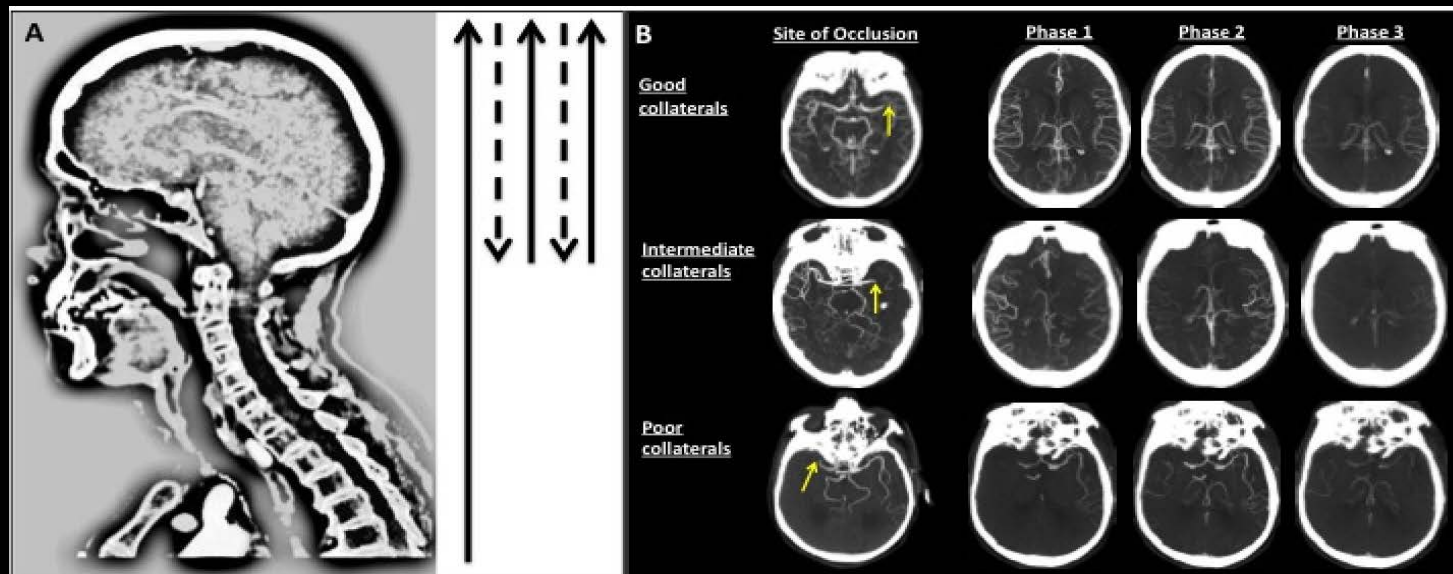


Collapsed axial thick MIP images.

Eligible occlusions for the ESCAPE trial:

- intracranial 'T' or 'L' ICA occlusion
- M1 occlusion
- M1 equivalent (all M2s)

Imaging – multiphase CTA (mCTA)



mCTA gives:

1. Easy and reliable assessment of collaterals
2. Very fast acquisition and fully automated image reconstruction
3. Less sensitive to patient motion
4. Easy to learn and interpret

(Radiology. 2015 Jan 29:142256. [Epub ahead of print])

Multiphase CTA

copies for distribution to your colleagues or clients, contact us at www.rsnid.org/itsnairights.

Multiphase CT Angiography: A New Tool for the Imaging Triage of Patients with Acute Ischemic Stroke¹

Bijoy K. Menon, MD
Christopher D. d'Este, PhD
Emmad M. Qazi, BSc
Mohammed Almekhlafi, MD²
Leszek Hahn, PhD
Andrew M. Demchuk, MD
Mayank Goyal, MD

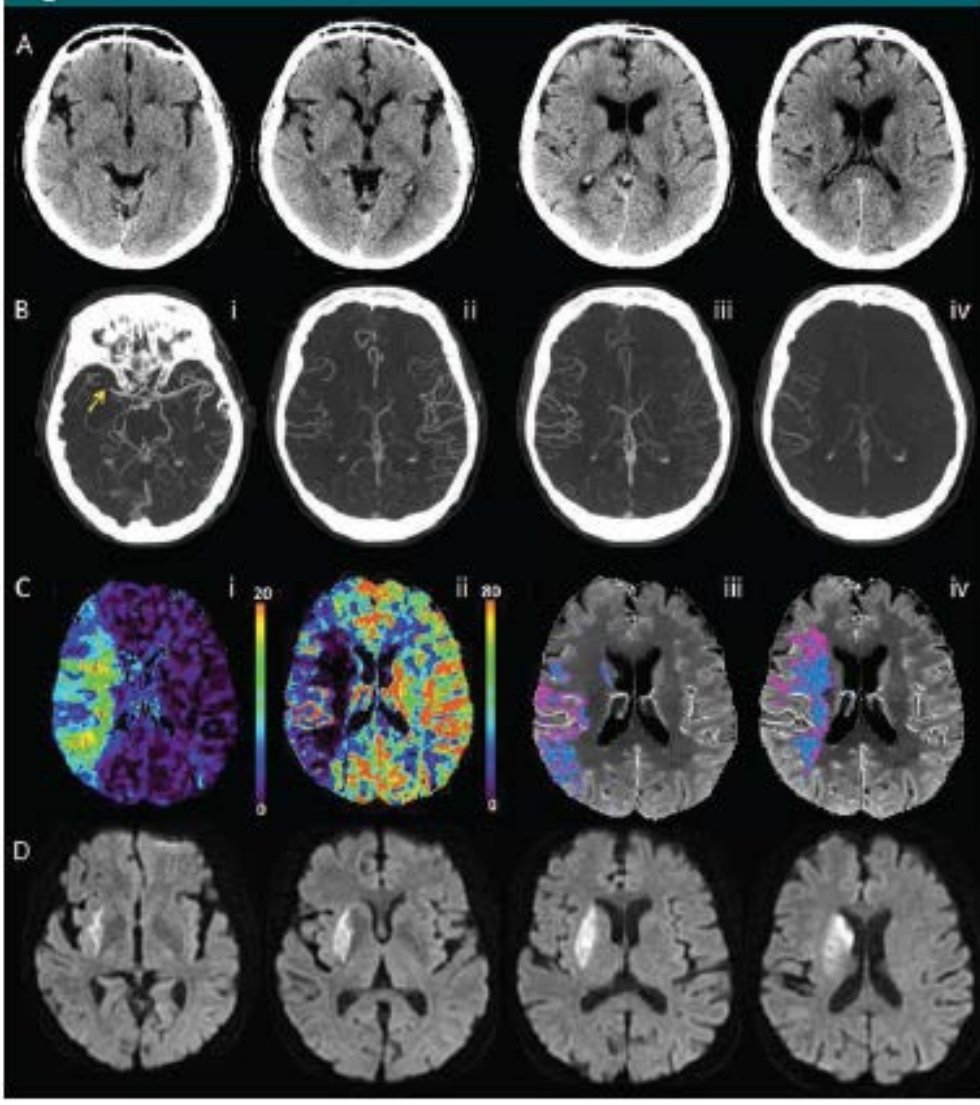
Purpose:

To describe the use of an imaging selection tool, multiphase computed tomographic (CT) angiography, in patients with acute ischemic stroke (AIS) and to demonstrate its interrater reliability and ability to help determine clinical outcome.

Materials and Methods:

The local ethics board approved this study. Data are from the pilot phase of PROveIT, a prospective observational study analyzing utility of multimodal imaging in the triage of patients with AIS. Patients underwent baseline un-

Figure 6



NCCT/MCTA :98 minutes from onset

78 WF, NIHSS 18; R hemisphere CT ASPECTS score is 8.

Proximal right M1 MCA occl

MCTA: a one phase delay, with similar extent and prominence to contralateral side.

A CBF-defined: infarct core is 113 mL (blue) and mismatch ratio (blue/pink areas) is 1.7; this indicates the patient should not undergo treatment.

Low % Imaging Protocol Deviations

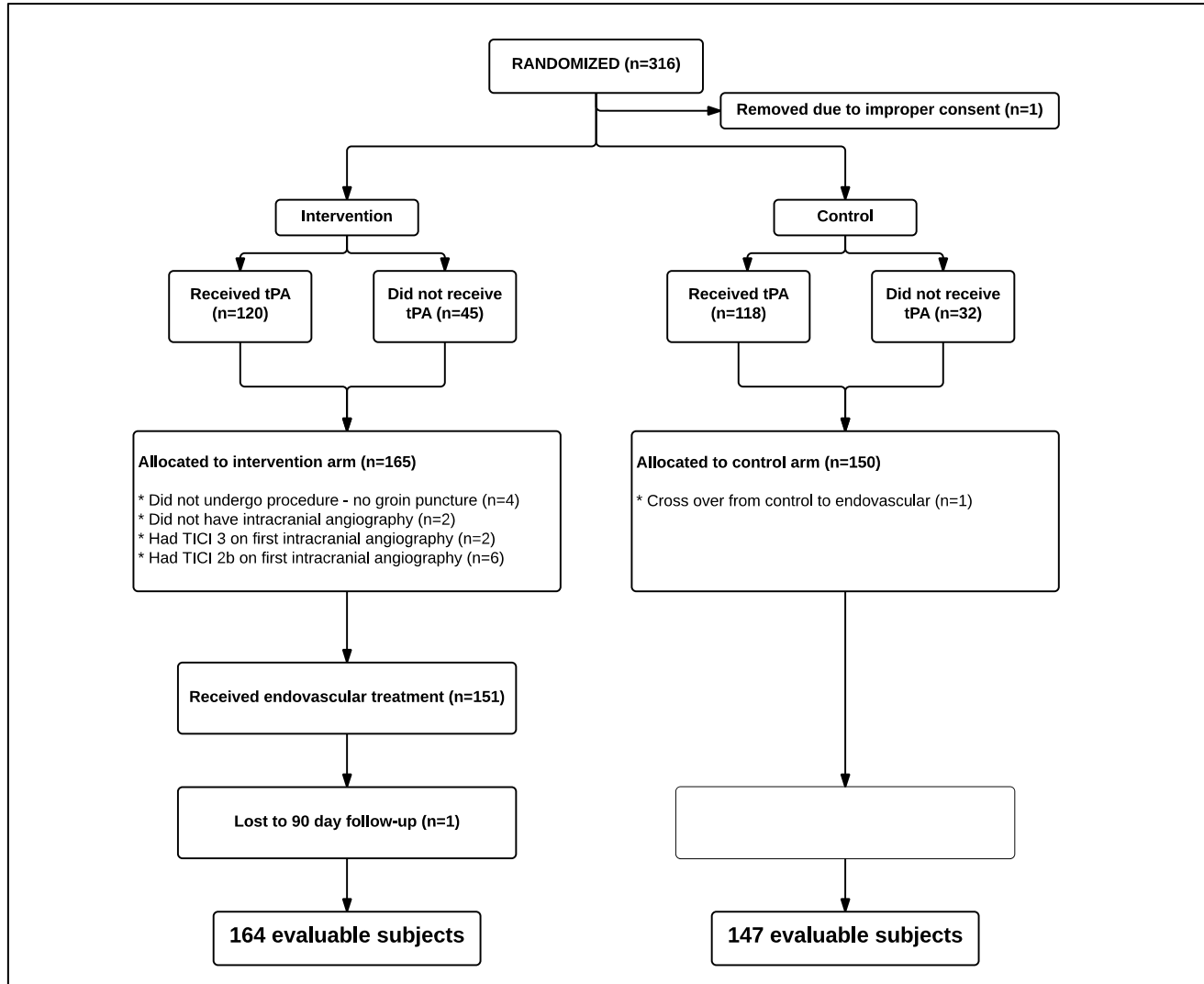
Sites interpretation: all appropriate

Core Lab:

ASPECTS		CTA occlusion		Collaterals
3.6%		4.5%		6.5%
ASPECTS 5	n=5	M2-MCA	n=9	Poor collaterals (<50% of the MCA territory)
ASPECTS 4	n=3			
ASPECTS 3	n=1	ICA, no MCA	n=5	

Results

- After MR CLEAN results were presented at the WSC, the trial steering committee suspended recruitment in the trial
- The planned interim analysis was conducted several weeks early
- The trial was then halted at the recommendation of the DSMB because the efficacy boundary had been crossed



Baseline Characteristics

Demographics	Intervention (N=165)	Control (N=150)
Age yr – median (IQR)	71 (60-81)	70 (60-81)
Female sex	52.1%	52.7%
Caucasian	87.3%	87.3%
Baseline NIHSS – median (IQR)	16 (13-20)	17 (12-20)
Hypertension	63.4%	72.0%
Diabetes Mellitus	20.0%	26.0%
Atrial fibrillation	37.0%	40.0%

Baseline Imaging

Imaging characteristics – (%)		Intervention (N=165)	Control (N=150)
CT ASPECTS median (IQR)		9 (8-10)	9 (8-10)
CTA occlusion location –(%)			
	ICA ‘T’ or ‘L’	27.6%	26.5%
	M1-MCA or both/all M2-MCA	68.1%	71.4%
	M2-MCA	3.7%	2.0%
Ipsilateral cervical carotid occlusion		12.7%	12.7%

Treatment Time Intervals

Process times min – median (IQR)	Intervention [N=165]	Control [N=150]
Symptom onset to randomization (N=315)	169 (117-285)	172.5 (119-284)
Onset to IV alteplase (N=237)	110 (80-142)	125 (89-183)
CT to groin puncture	51 (39-68)	---
CT to first reperfusion	84 (65-115)	---
Onset to first reperfusion	241 (176-359)	---
Treatment with IV alteplase	72.7%	78.6%



ANDREW

Safety Outcomes

	Intervention [n=165]	Control [n=150]	RR (CI ₉₅)	Adjusted § RR (CI ₉₅)
Death [N=311]	10.4%	19.0%	0.5 (0.3-0.95)	0.5 (0.3-0.8)
Large MCA/malignant MCA stroke	4.9%	10.7%	0.5 (0.2-1.0)	0.3 (0.1-0.7)
sICH (clinically determined at site)	3.6%	2.7%	1.4 (0.4-4.7)	1.2 (0.3-4.6)
Access site hematoma	1.8%	0%	---	---
MCA perforation	0.6%	0%	---	---

Angiographic Outcomes

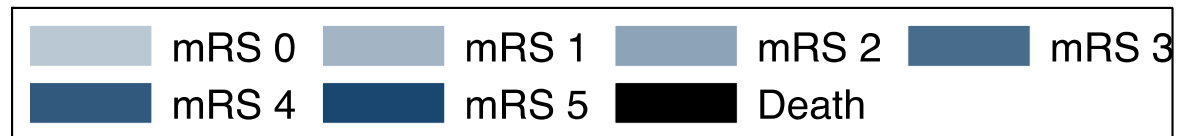
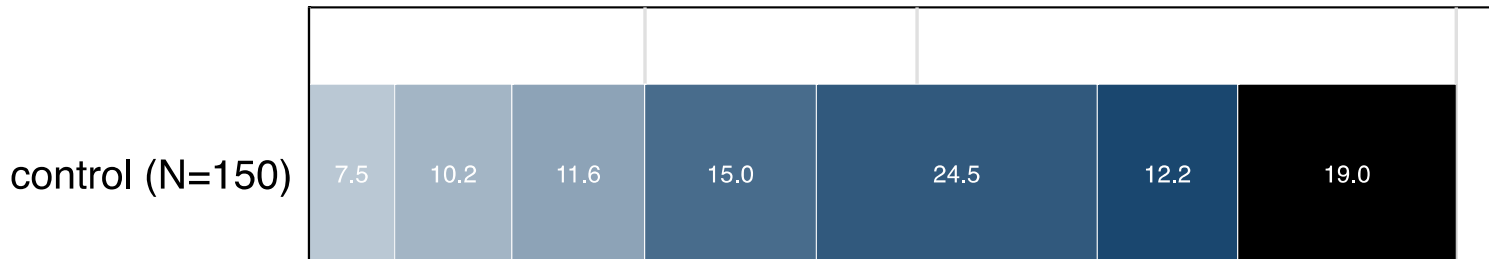
	Intervention	Control
Final Reperfusion TICI 2b/3 [Angio Core lab determined]	72.4%	---
mAOL 2-3 (at 2-8h CTA) [CT Core lab determined]	---	31.2%
Retrievable Stent Use	86.1%	

Outcomes (NNT = 4)

Clinical	Intervention [n=165]	Control [n=150]	RR or cOR (CI ₉₅)	Adj RR or cOR (CI ₉₅)
mRS primary outcome (“shift analysis”) [n=311]	---	---	2.6 (1.7-3.8)	3.1 (2.0-4.7)
mRS 0-2 at 90d [n=311]	53.0%	29.3%	1.8 (1.4-2.4)	1.7 (1.3-2.2)
EQ-VAS at 90d (median, iqr)	80 (30)	65 (30)	P<0.001 (rank sum test)	

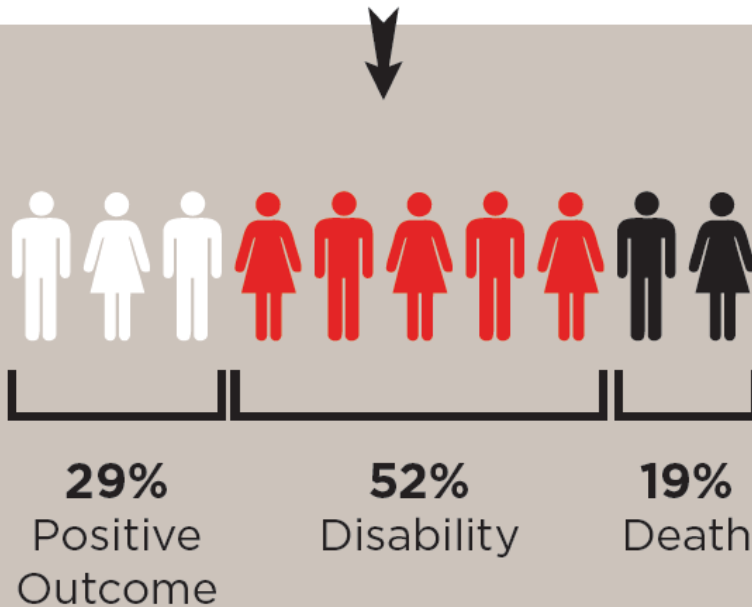
Overall ESCAPE trial results

Shift on 90-d mRS

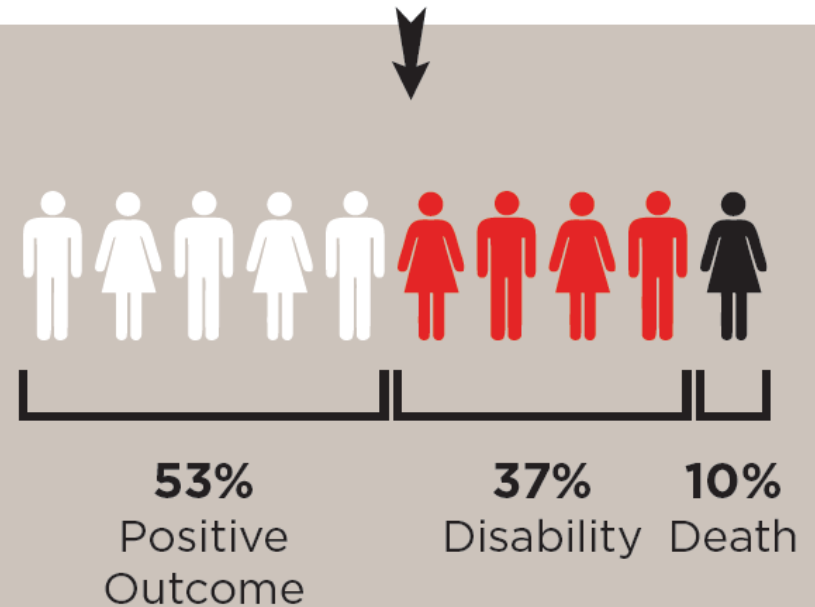


ESCAPE Outcomes

MEDICAL TREATMENT (No endovascular treatment)

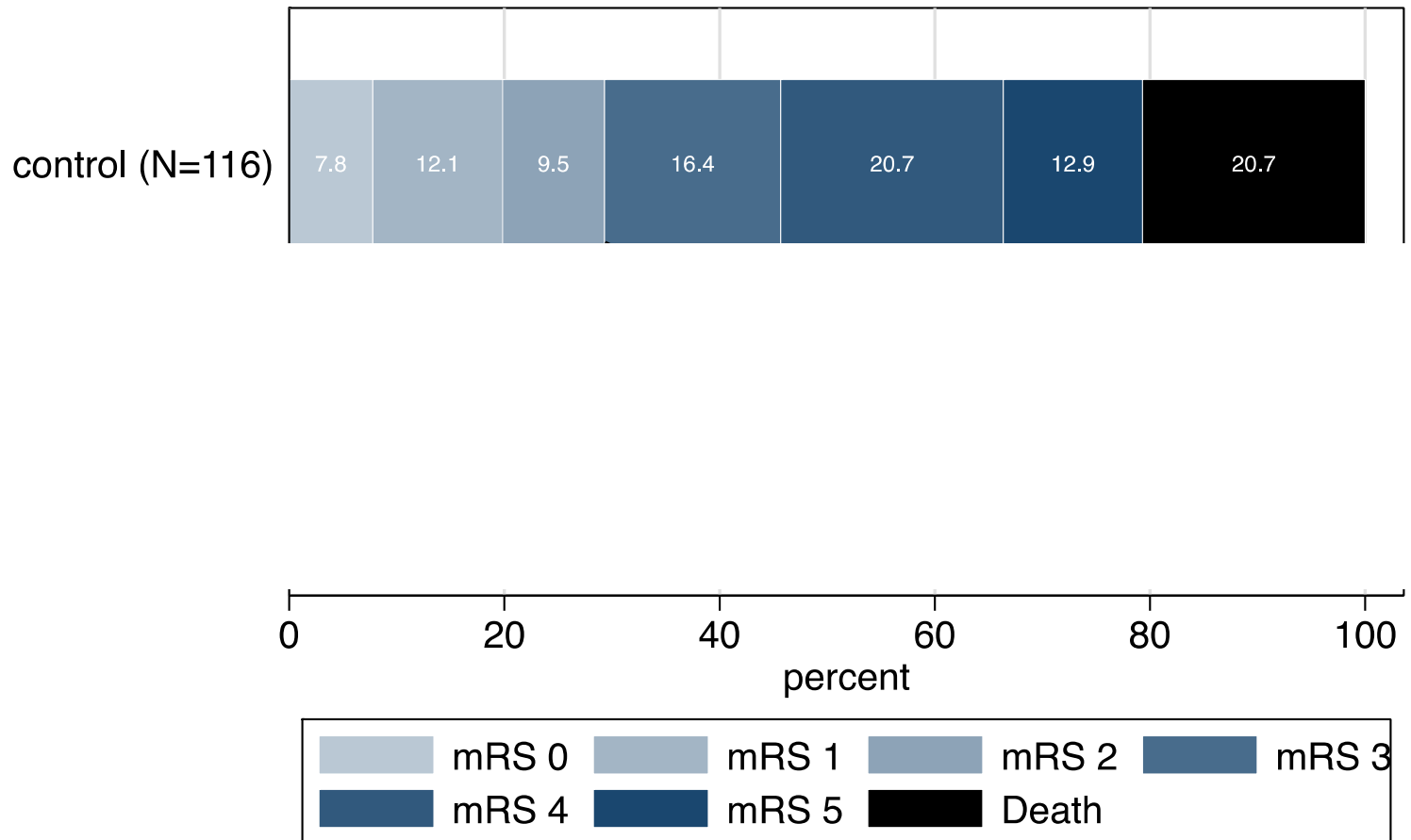


ENDOVASCULAR TREATMENT (With medical treatment)



IV tPA group [N=235]

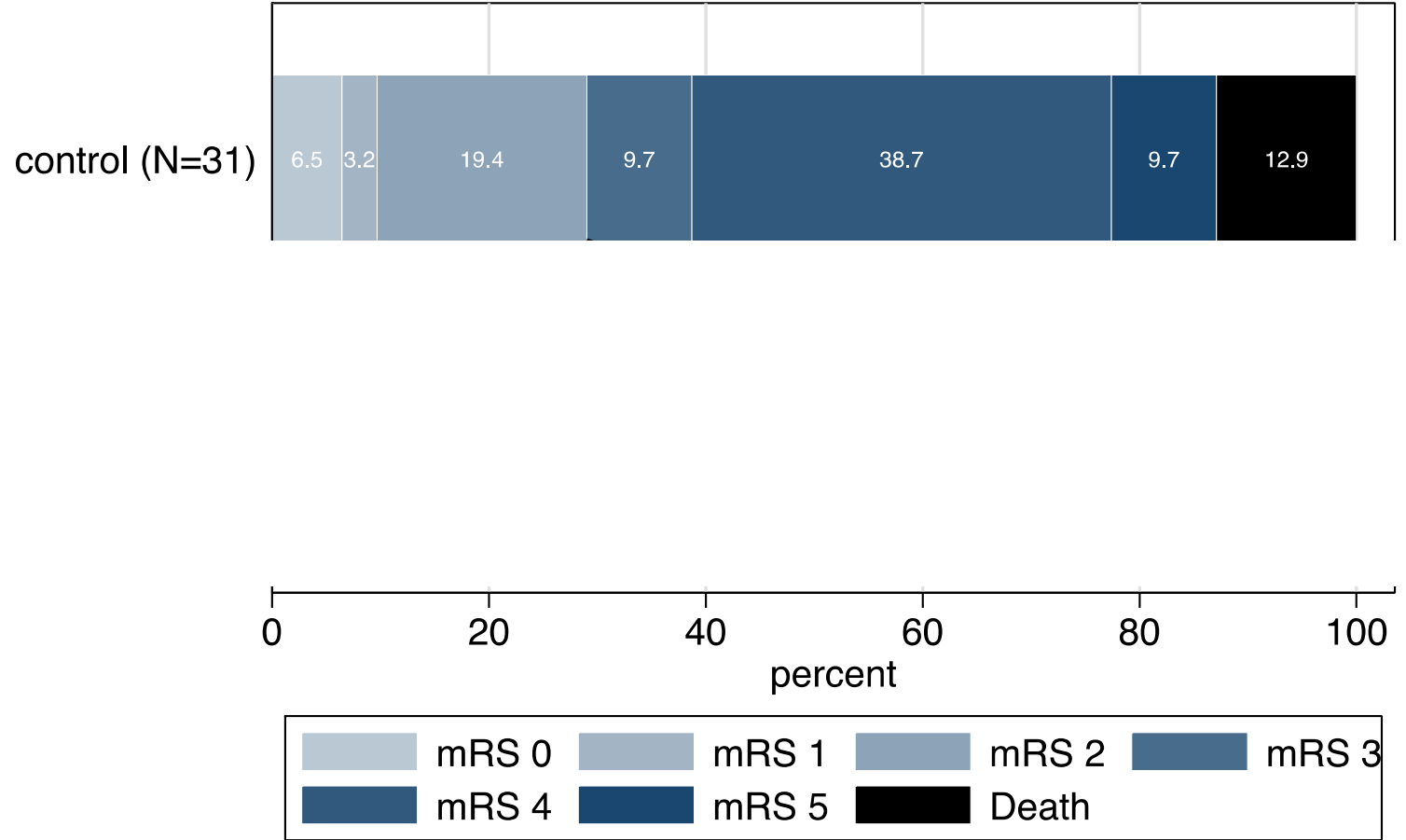
Shift on 90-d mRS



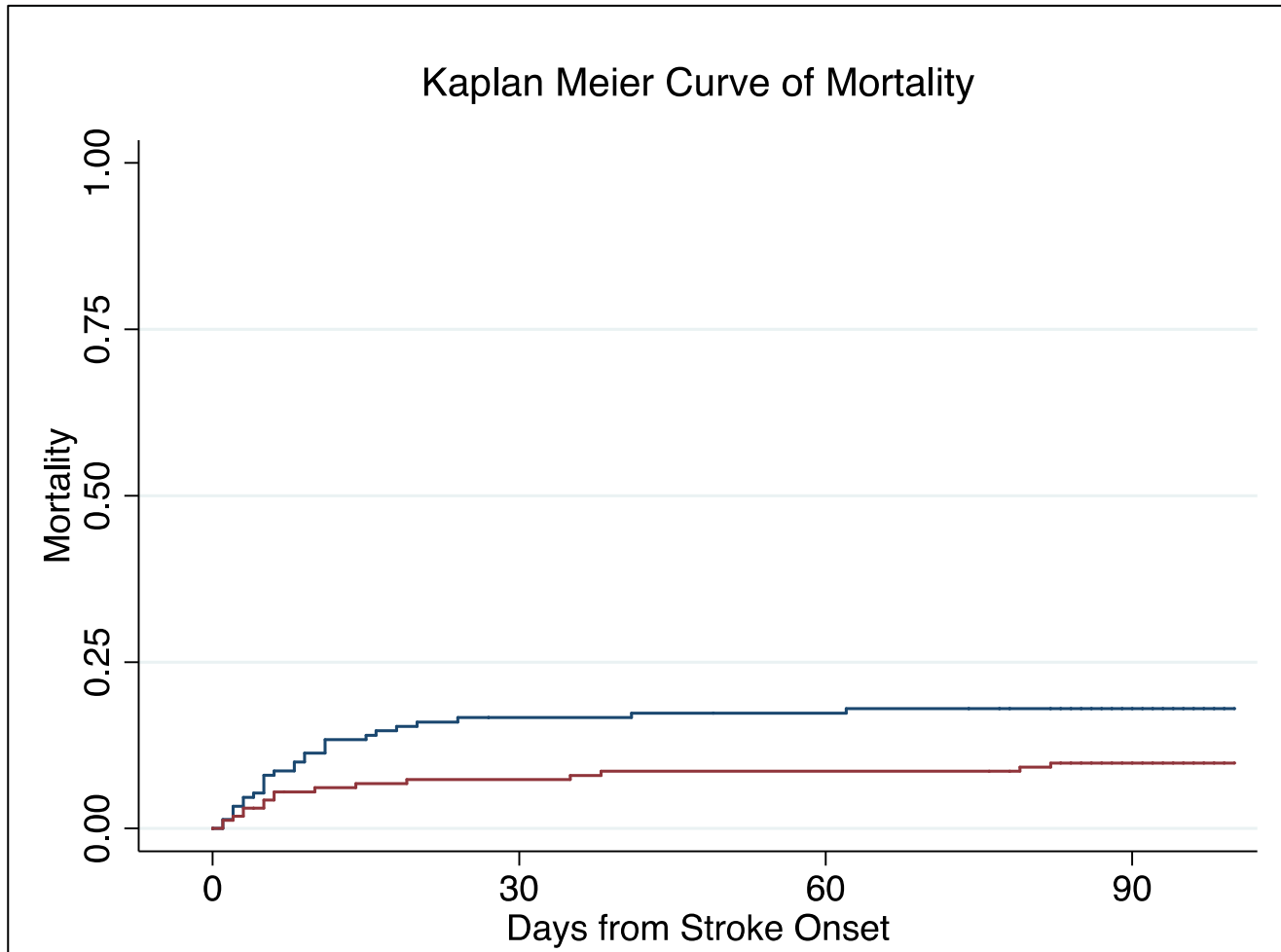
N=238, 3 lost to follow-up.

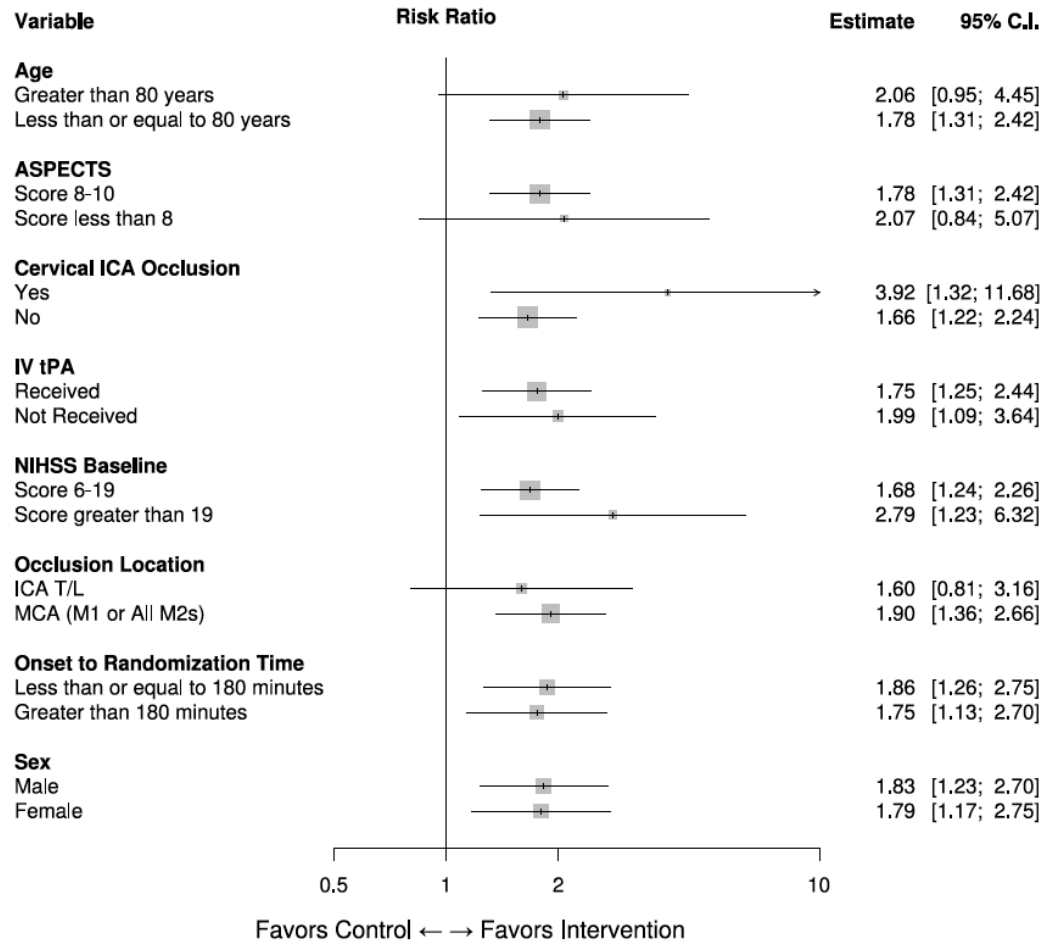
Non-IV tPA group [N=76]

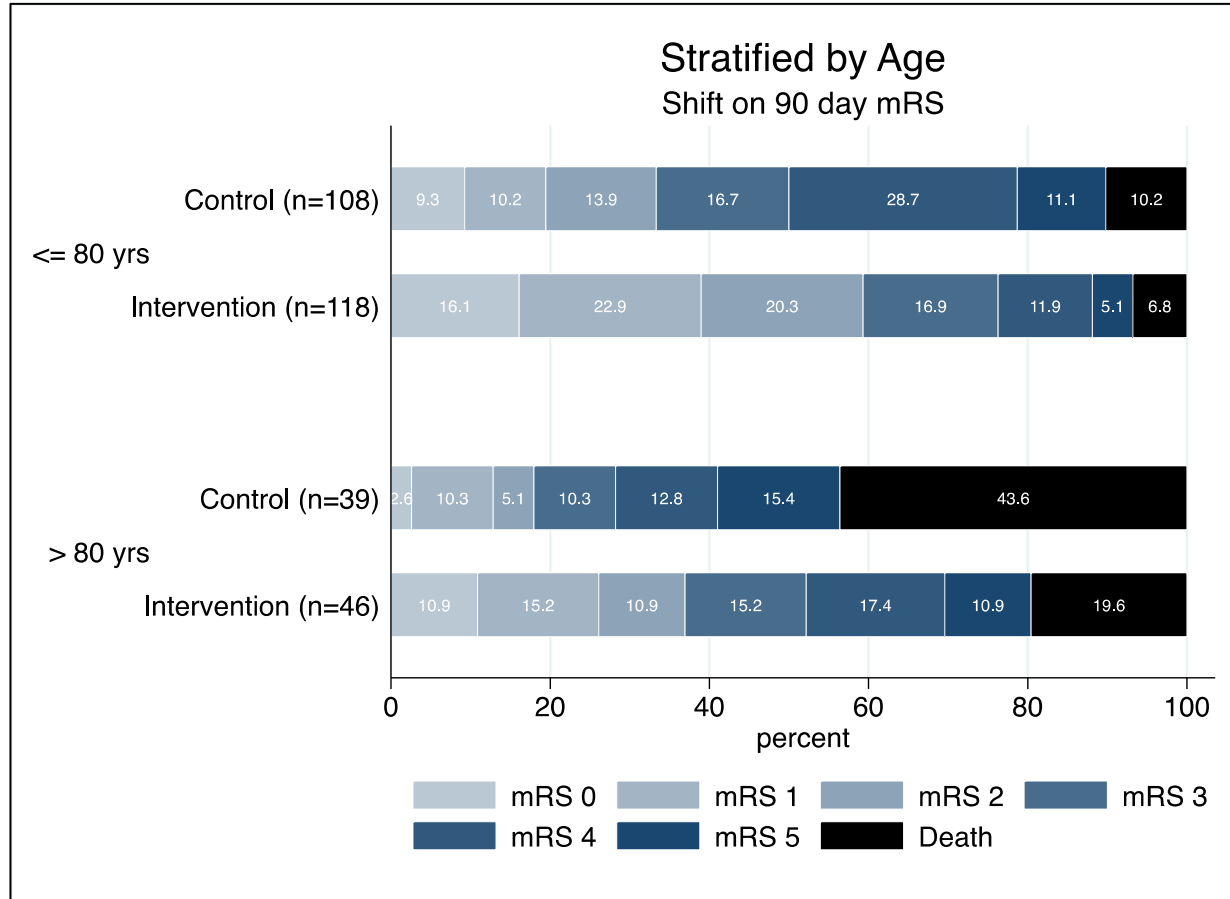
Shift on 90-d mRS

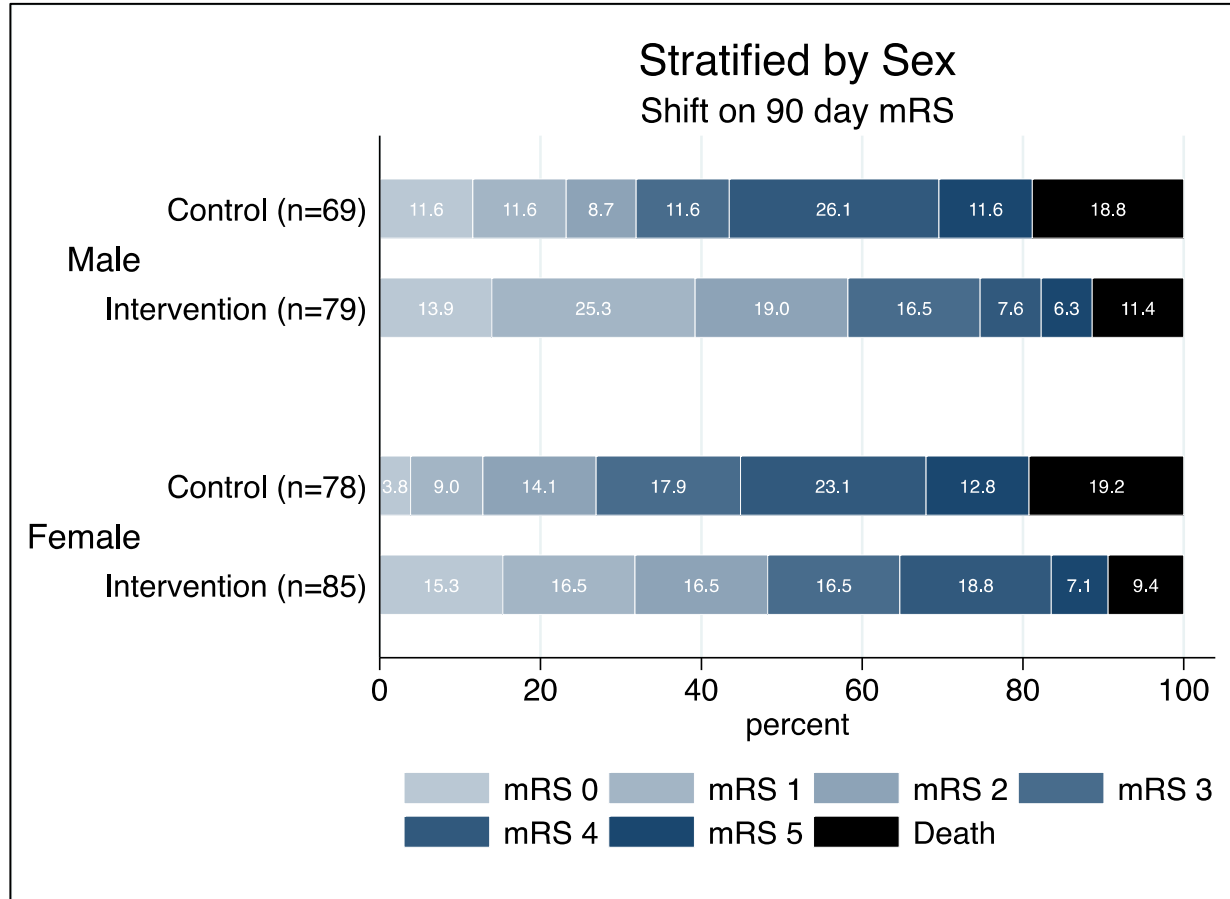


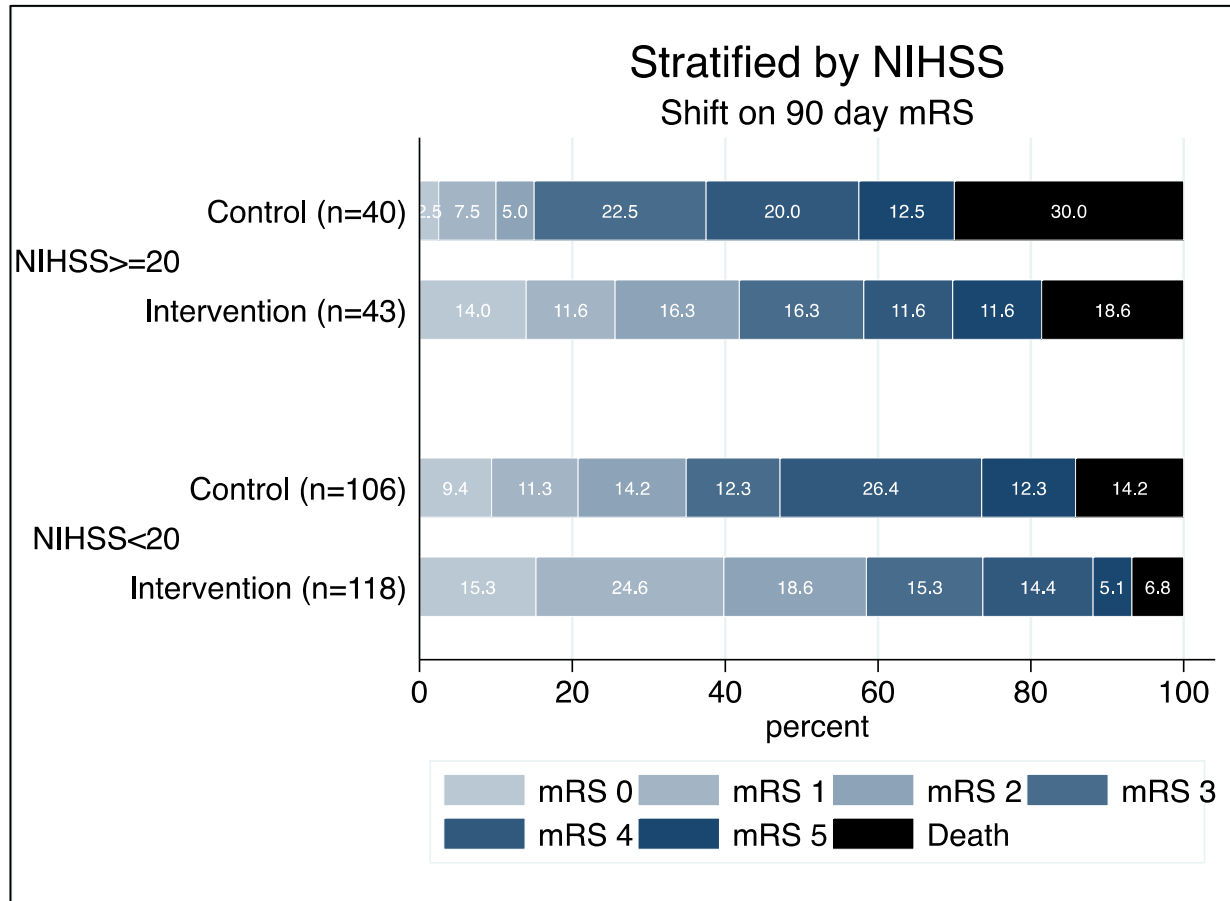
N=77, 1 lost to follow-up.

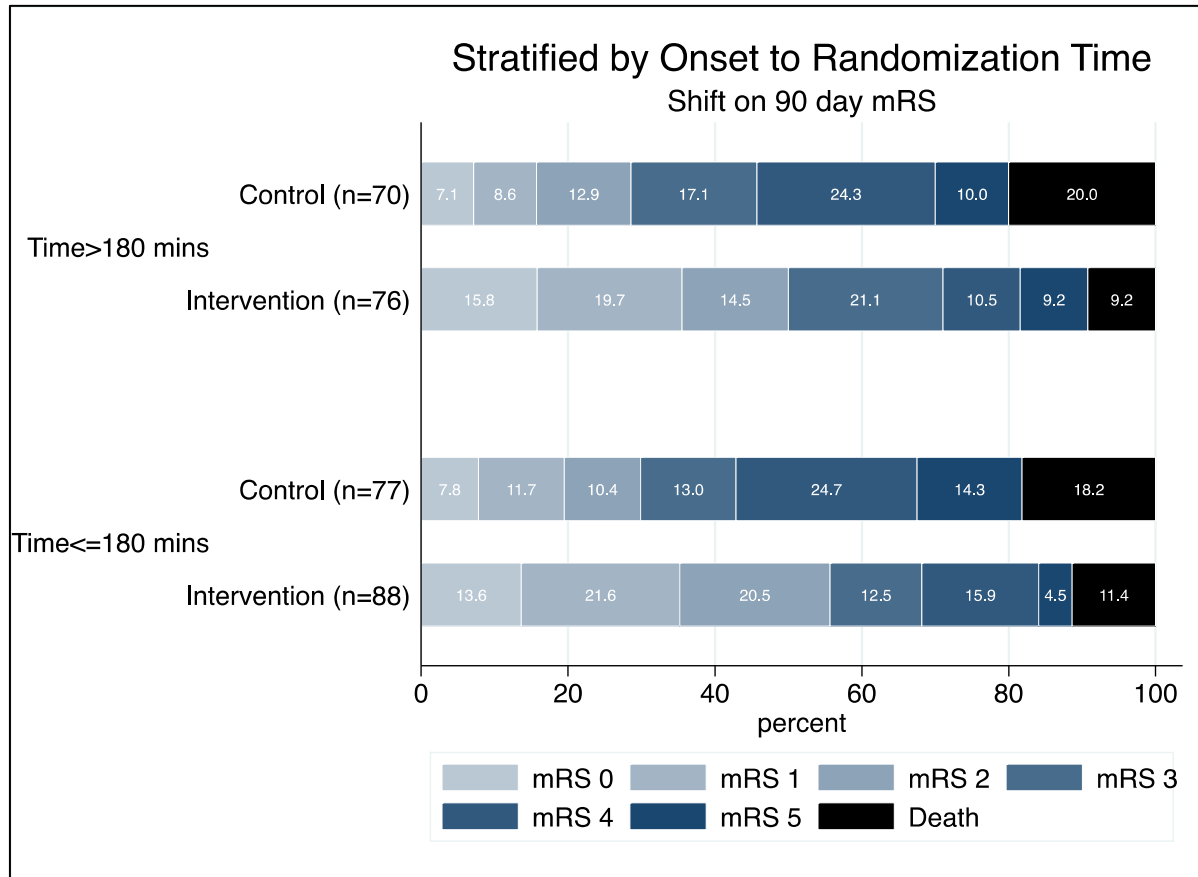




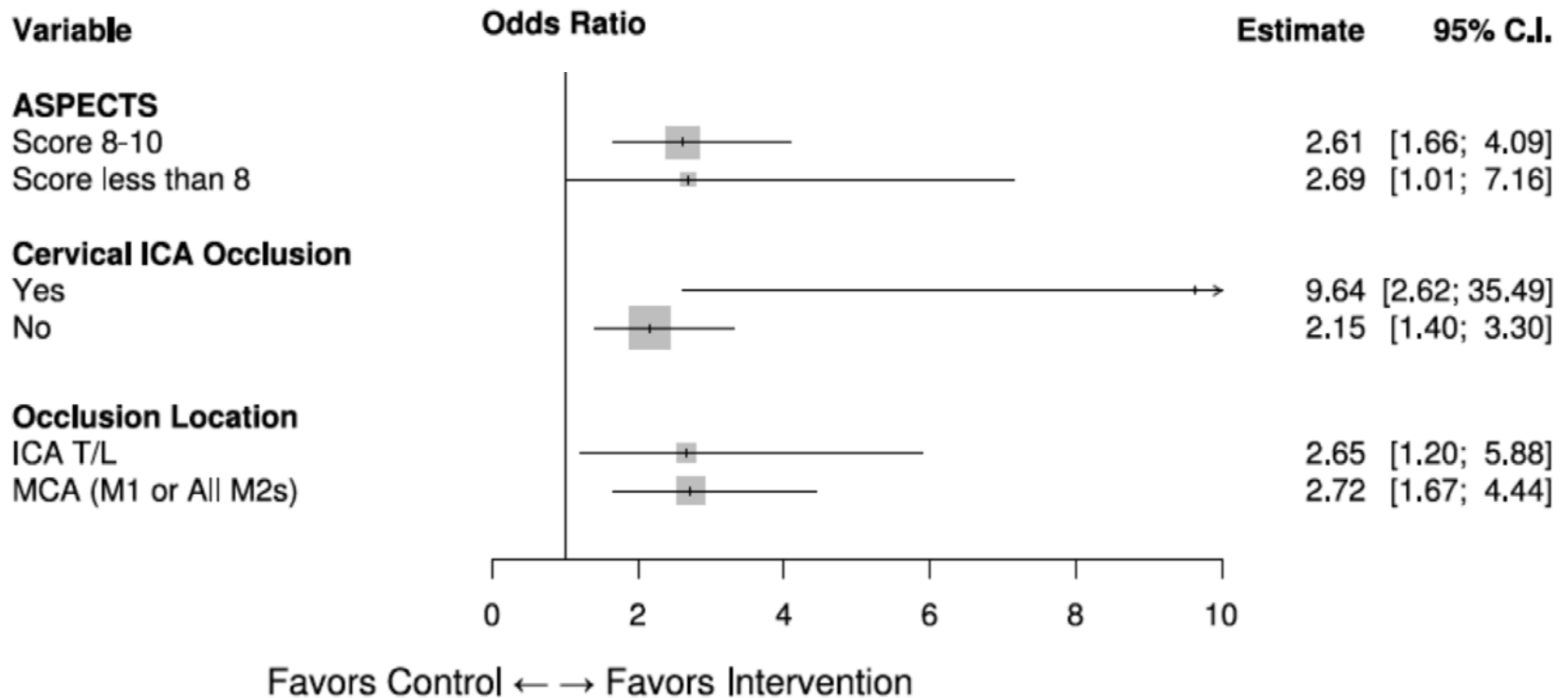


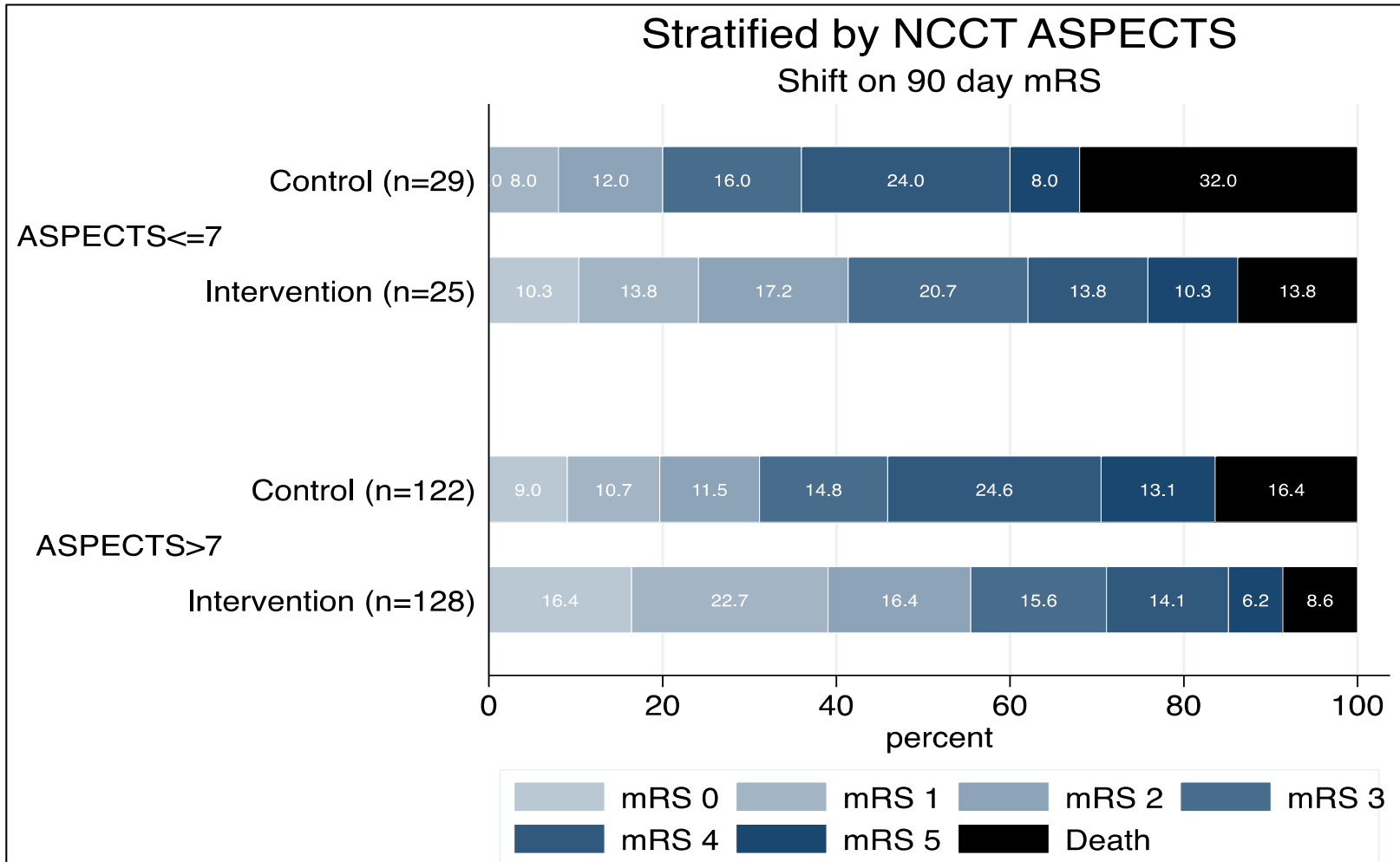




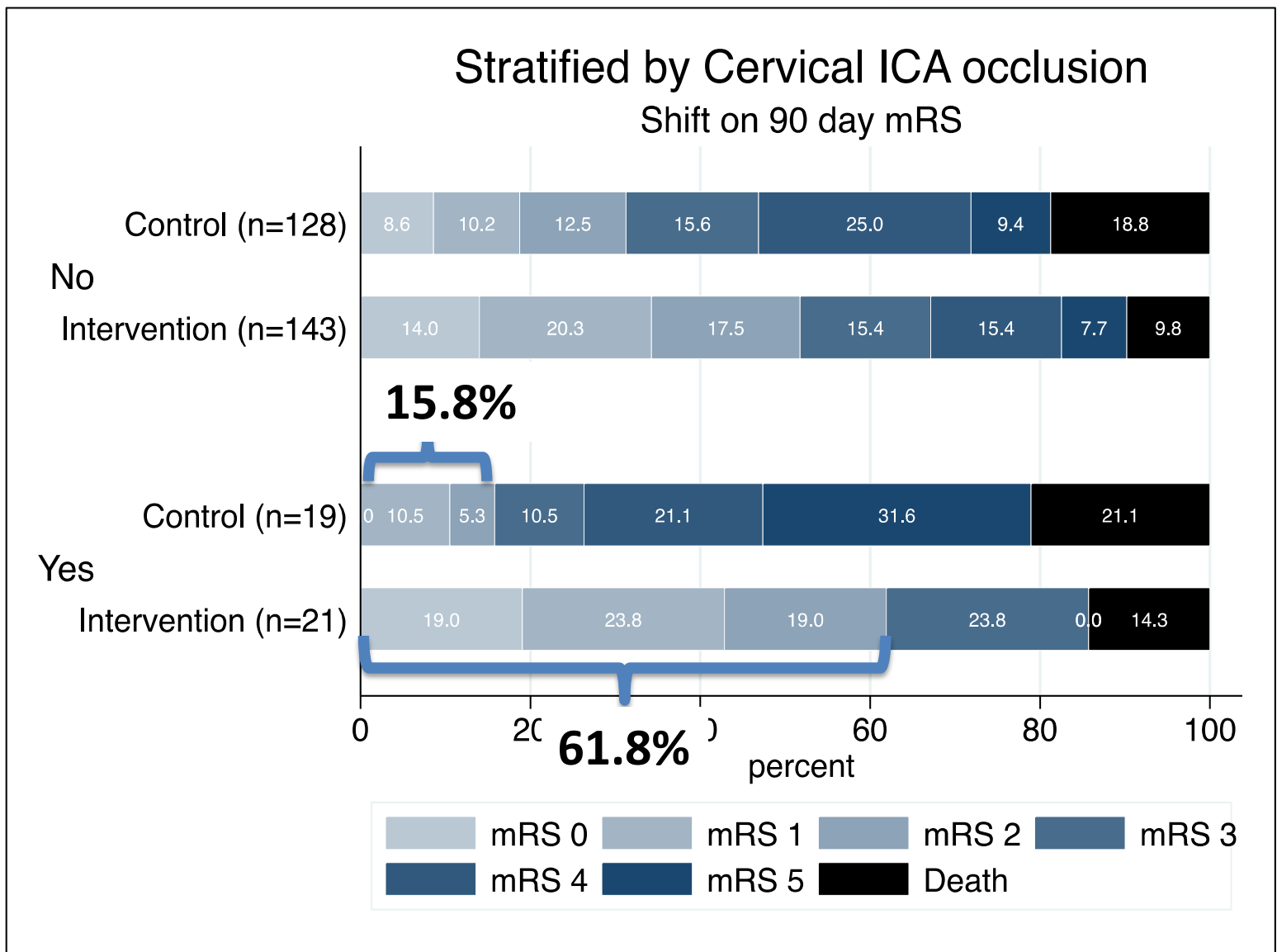


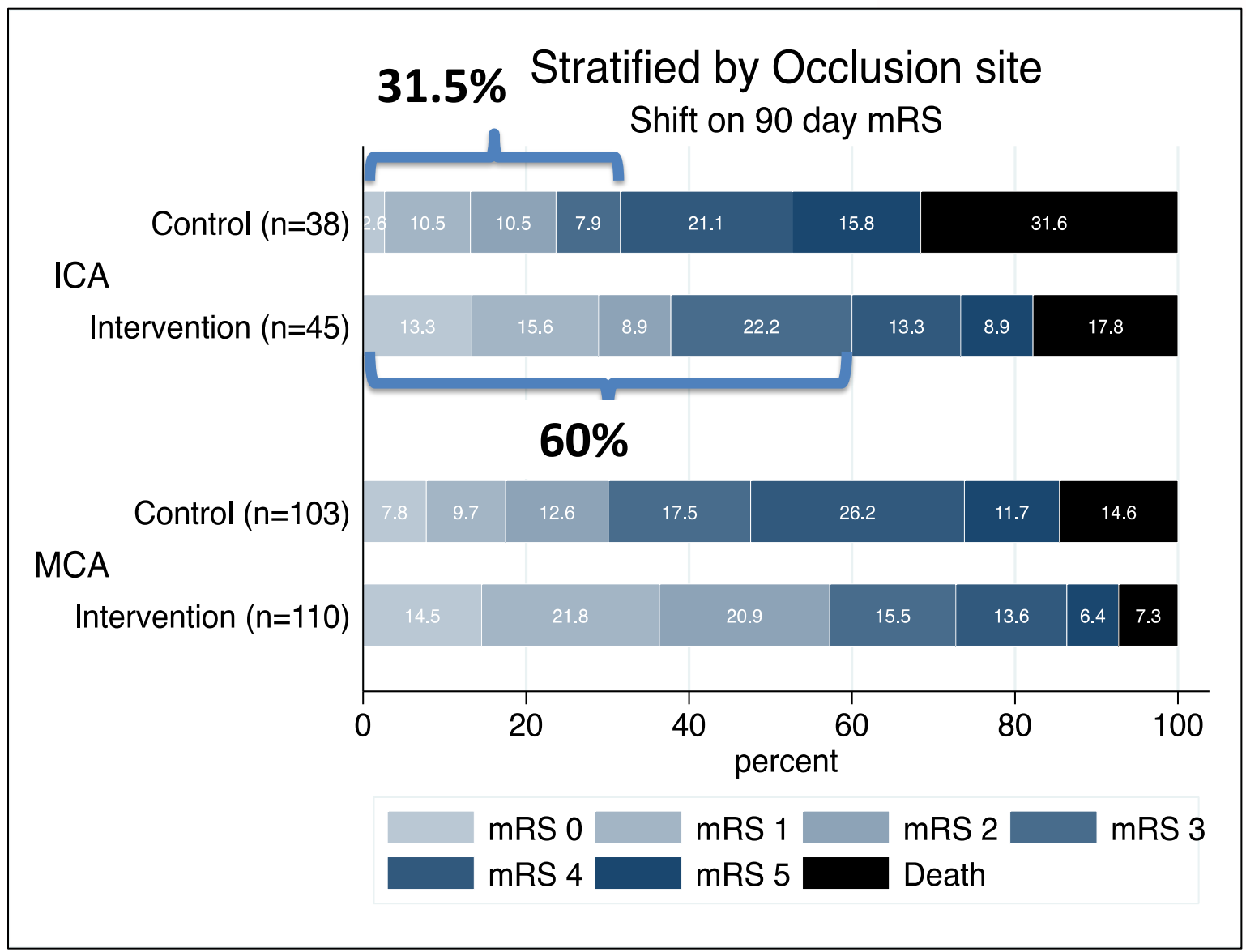
Imaging-Defined Sub-groups All Benefit





Supplementary Figure 7b: Figure shows benefit in the intervention group when compared to the control group across the 90-day mRS distribution in subjects with baseline non-contrast CT ASPECTS ≤ 7 vs. > 7 . **Nine subjects had CT ASPECTS 0-5 (protocol violators) and are included in the ASPECTS ≤ 7 group for this analysis.** Threshold for ASPECTS was pre-defined. There is no evidence of heterogeneity of treatment effect between these subgroups. ($p_{interaction}=0.914$, Wald test).





Effect size for Intervention

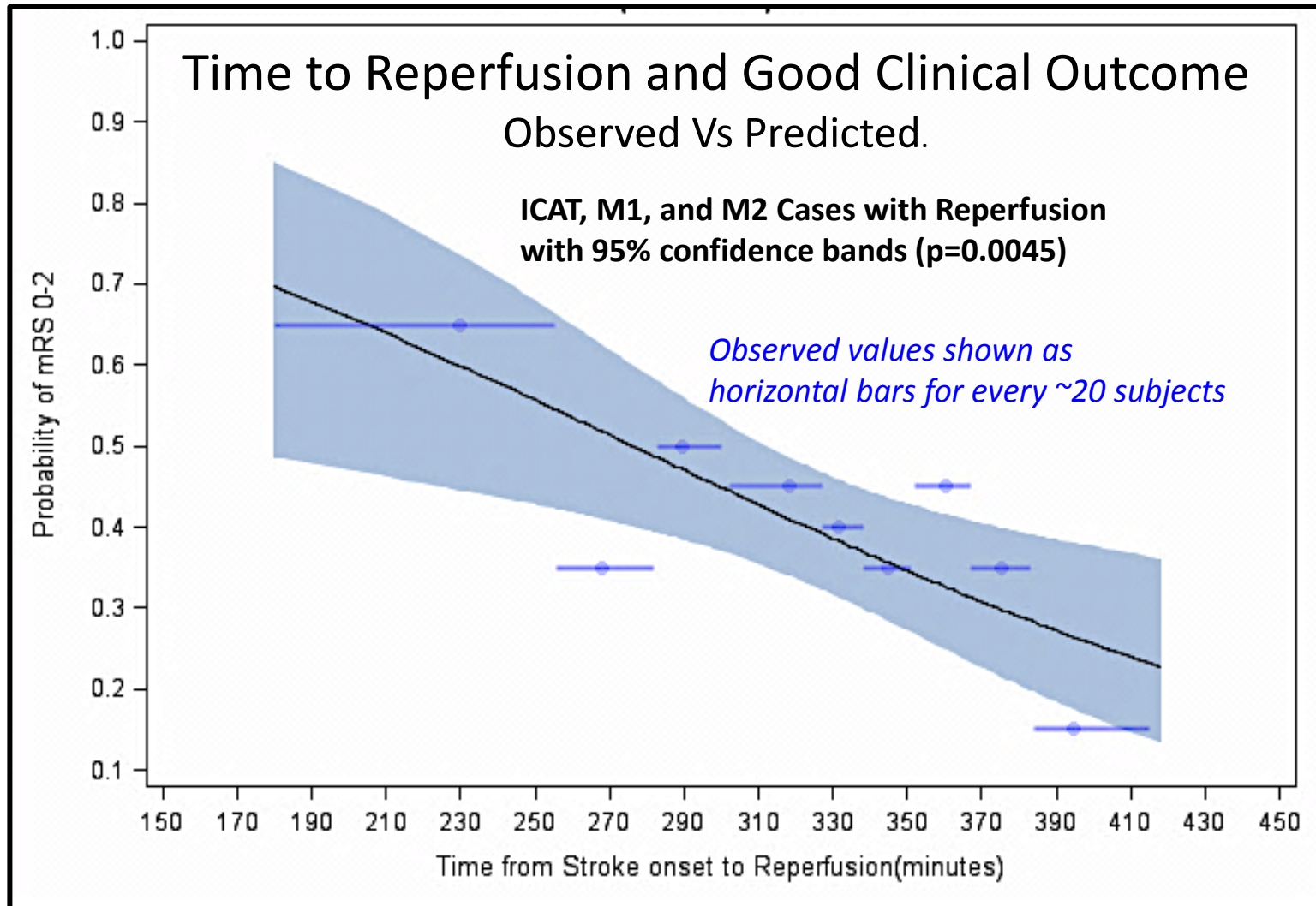
common OR* (“shift”) 3.1 (2.0-4.7)

mRS 0-2 29.3% → 53.0% NNT = 4

Death HR* 19.0% → 10.4% 0.4 (0.2-0.8)

*Adjusted for age, sex, baseline NIHSS score, baseline ASPECTS score, IV alteplase use, baseline occlusion location

Workflow: Time is brain



Comparing Interval Times

	ESCAPE	MR CLEAN	IMS III	SYNTHESIS
Onset→ Randomization	171 min (IQR 118-285)	204 min (IQR 152-251)	~135 min	~146 min
Onset→ IV tPA	114 min (IQR 82-160)	85 min (IQR 67-110)	~111 min	165 min (IQR 140-200)
Onset→ Groin Puncture	200 min (IQR 144-315)	260 min (IQR 210-313)	~196 min	~225 (?200) min**
Onset→ Reperfusion	241 min (IQR 176-359)	---	~321 min	---

**Onset-to-treatment (eg. infusion of intra-arterial tPA)

NEJM. 2015; 372(1): 11-20.; NEJM 2013: 368(25): 2433-34; Circulation. 2014;130:265-272

Comparing Interval Times

	ESCAPE	IMS III
CT→ Groin Puncture “Picture to puncture”	51 min	~107 min.
CT→ Reperfusion “picture to perfusion”	84 min	~232 min

- Picture = first slice non-contrast CT
- ESCAPE patients were first encountered at similar times to prior trials but were effectively treated much faster

Circulation. 2014;130:265-272

Reperfusion

	Intervention		Control	
	IV tPA	No IV tPA	IV tPA	No IV tPA
TICI 2b/3	70.5%	77.3%	---	---
mAOL 2-3	---	---	37.3%	7.1%

mAOL assessed on CTA done at 2-8h post randomization

Comparing Reperfusion

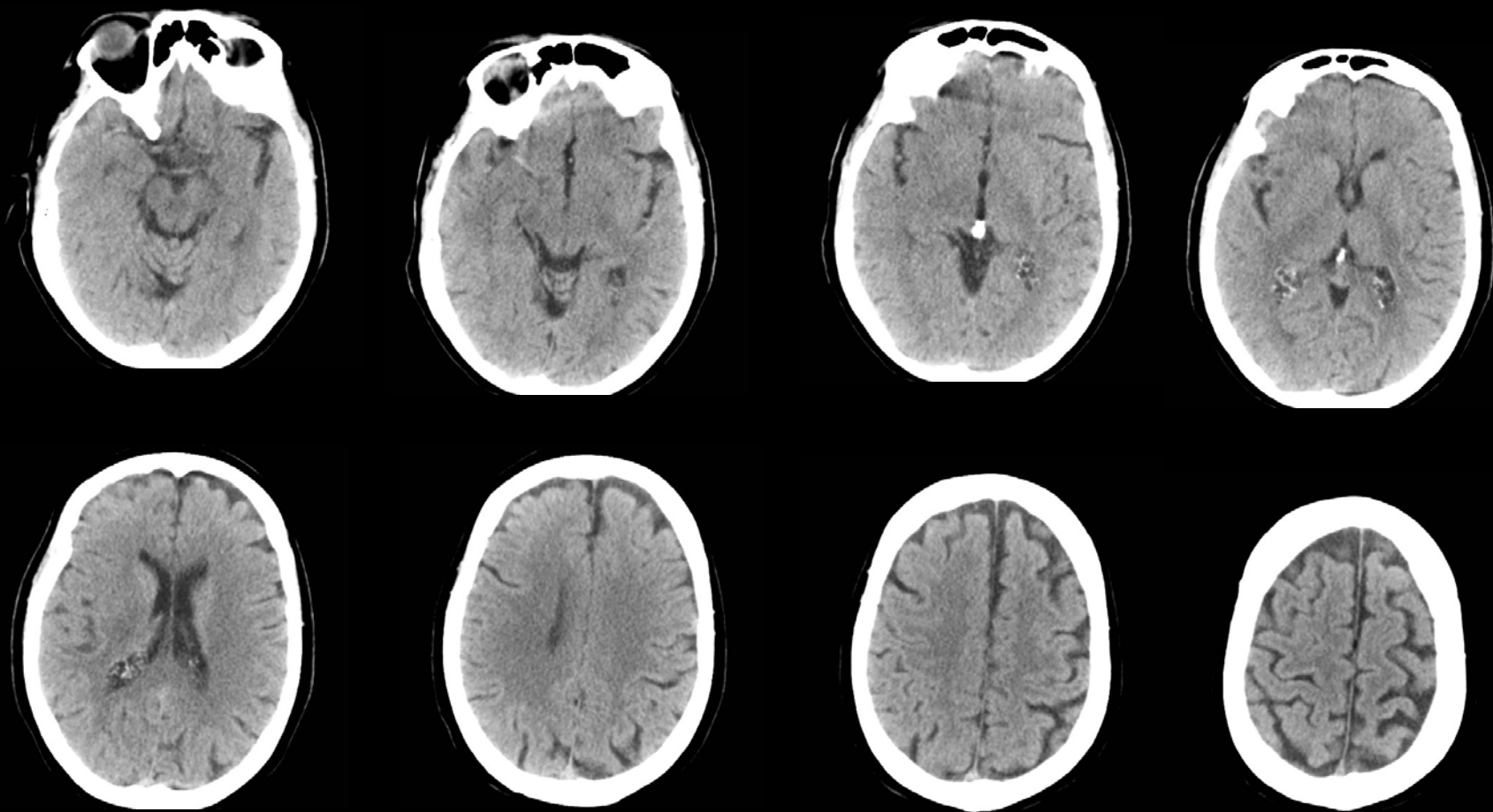
	ESCAPE	MR CLEAN	IMS-III
TICI 2b/3	72.6%	58.7%	45.2%

- Higher rates of reperfusion with current technique and devices
- Early assessment of the control group (2-8h in ESCAPE) shows only modest rates of reperfusion in the control group; 24h assessment time is too late

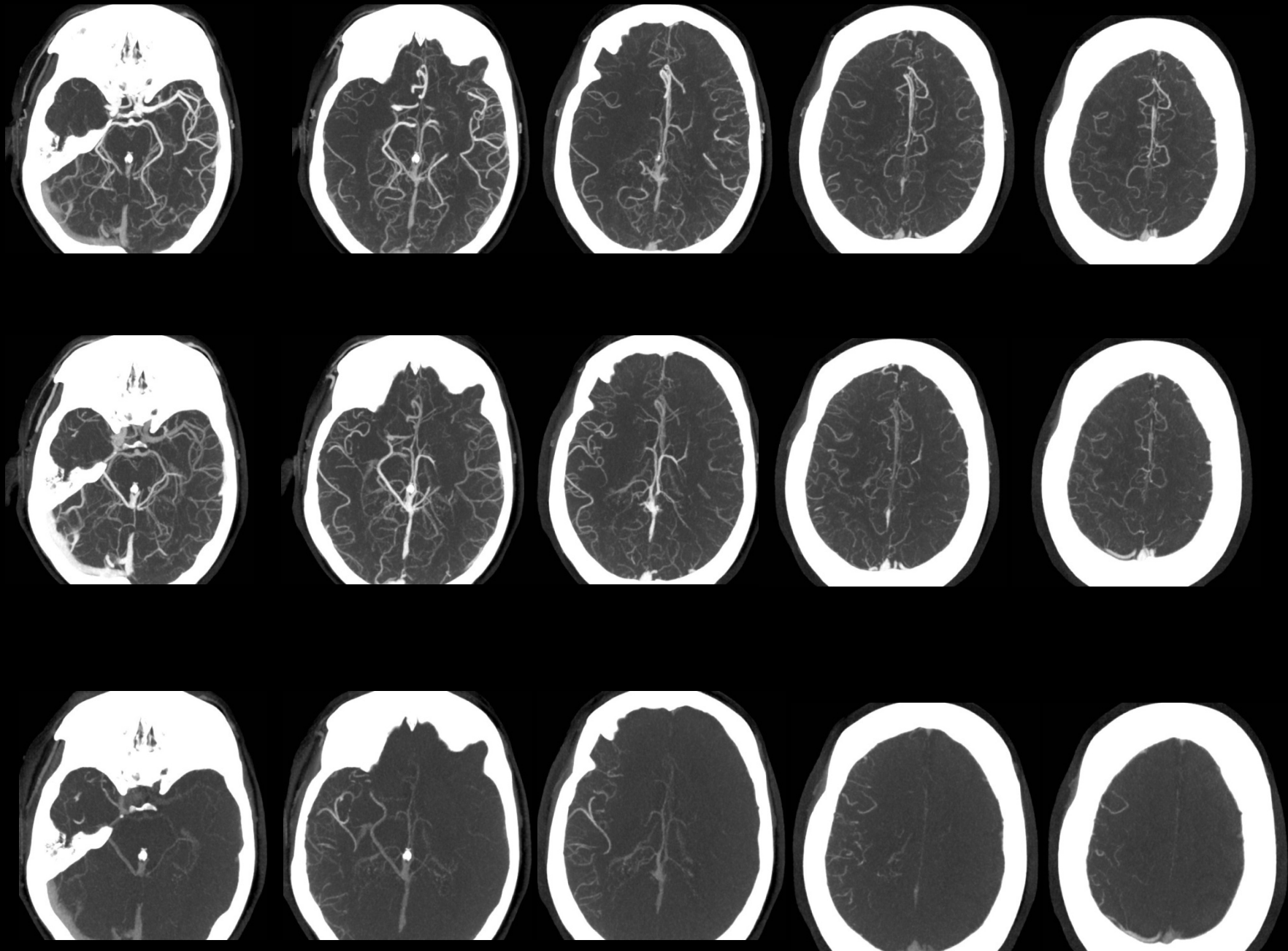
Illustrative Case

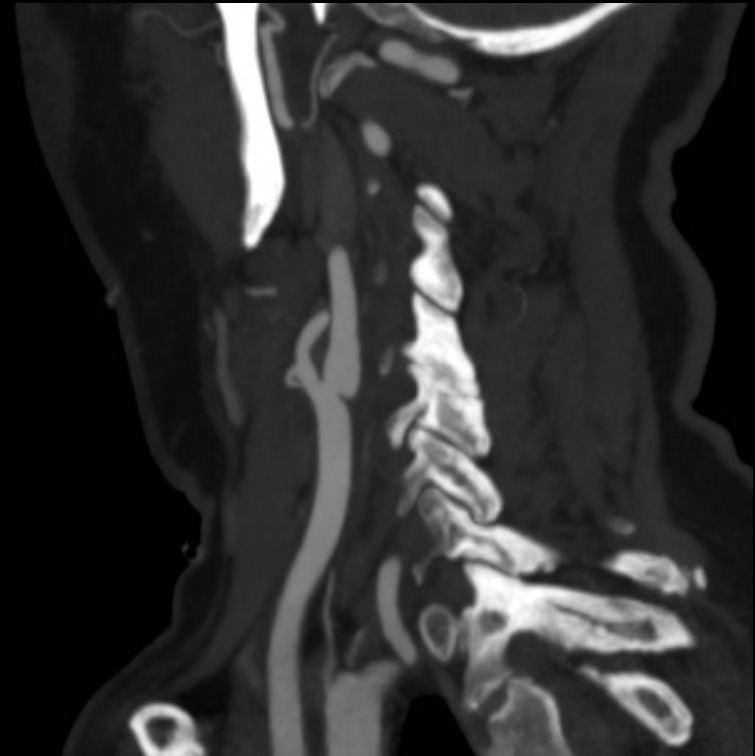
- NIH 18
- Otherwise healthy
- Eligible for trial
- 65 min from onset

1220



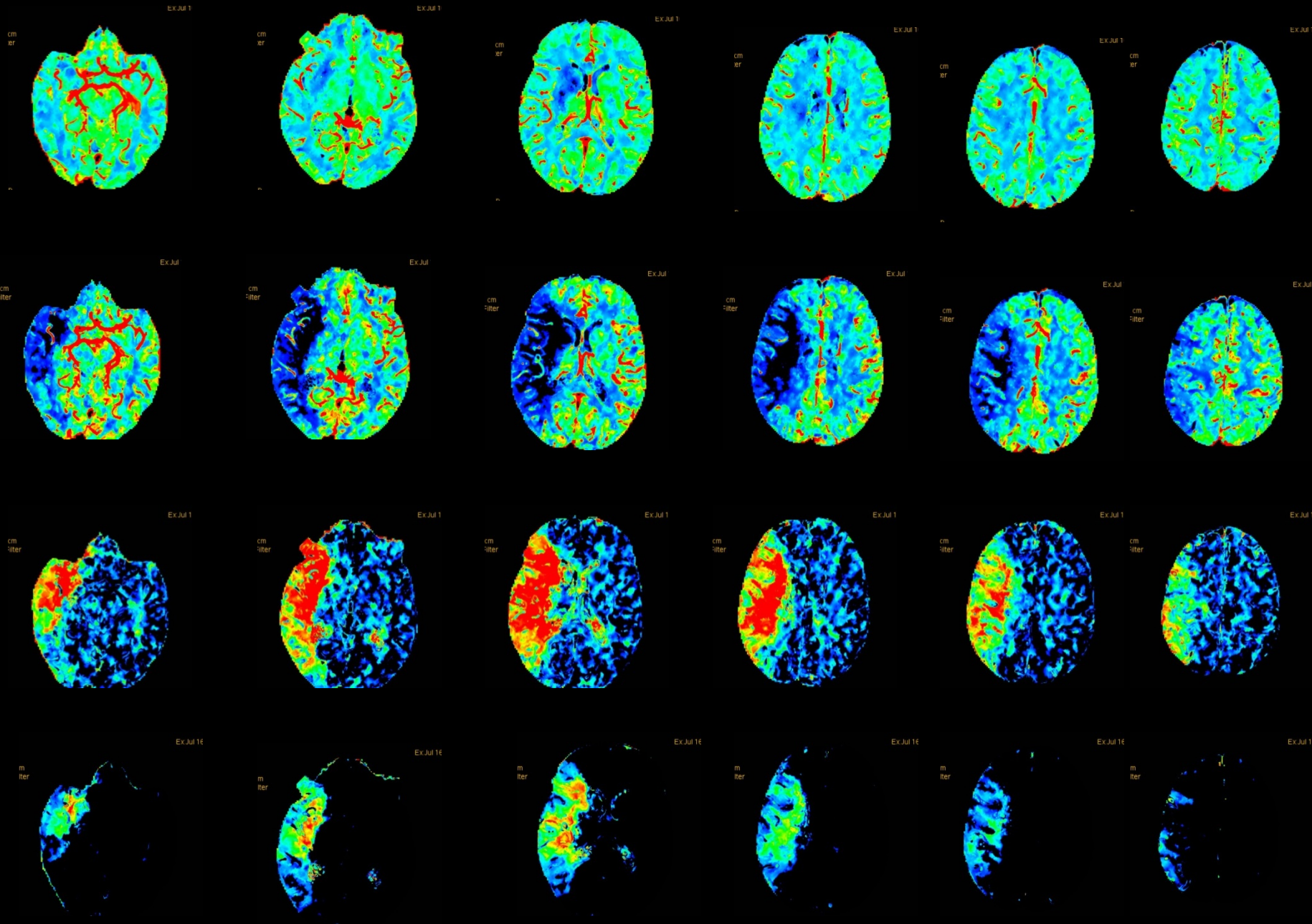
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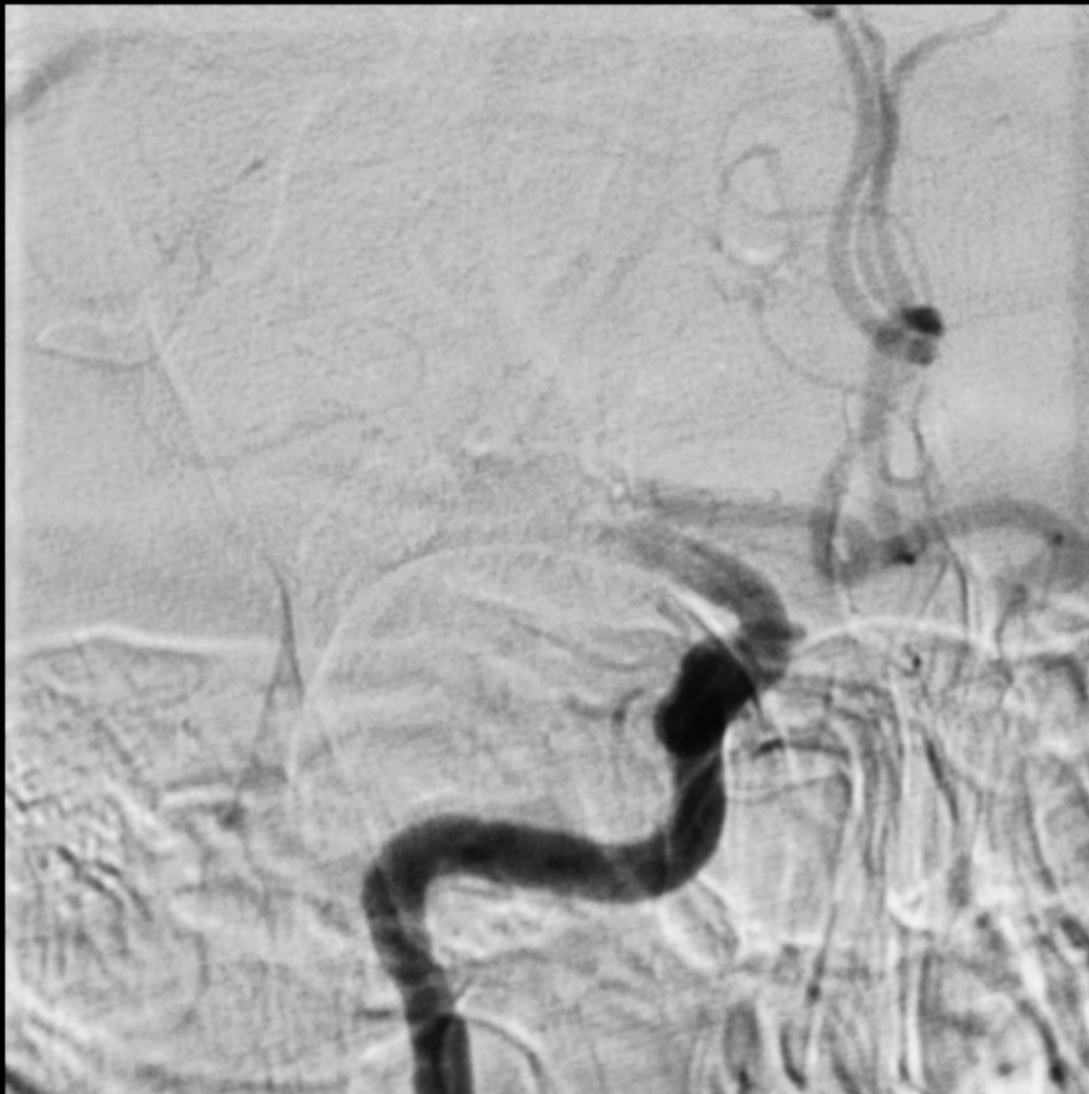


Parallel processing

Team divides: one part goes to talk to family; I go to angio



1241



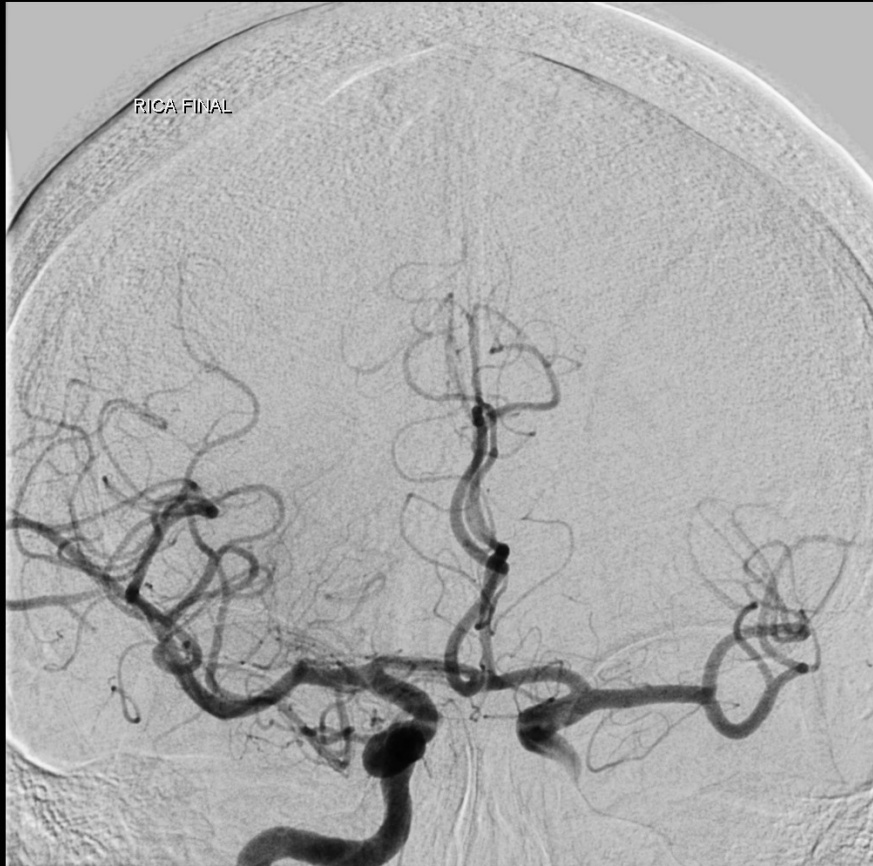
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Solitaire 4 by 40

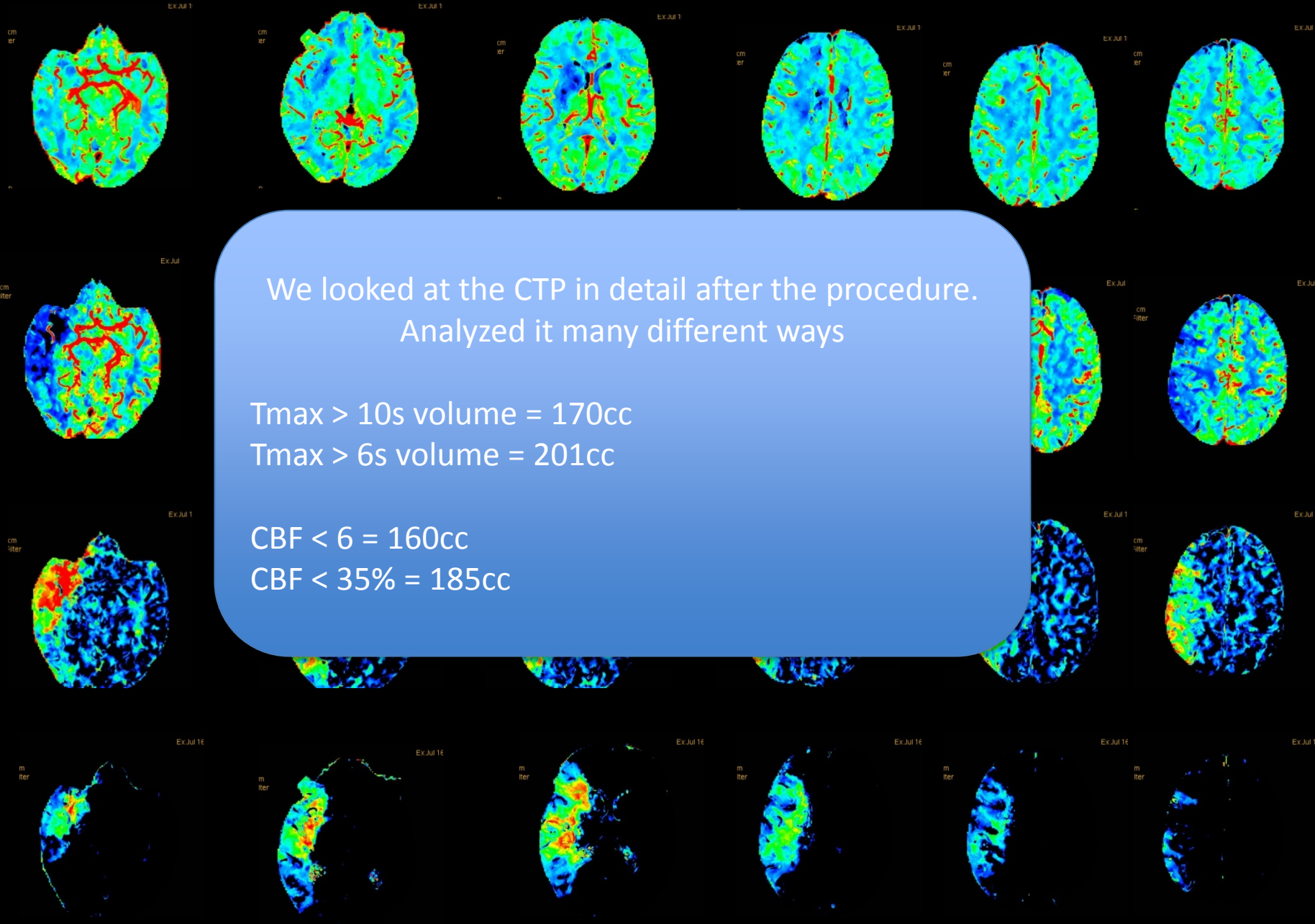
Patient starts improving



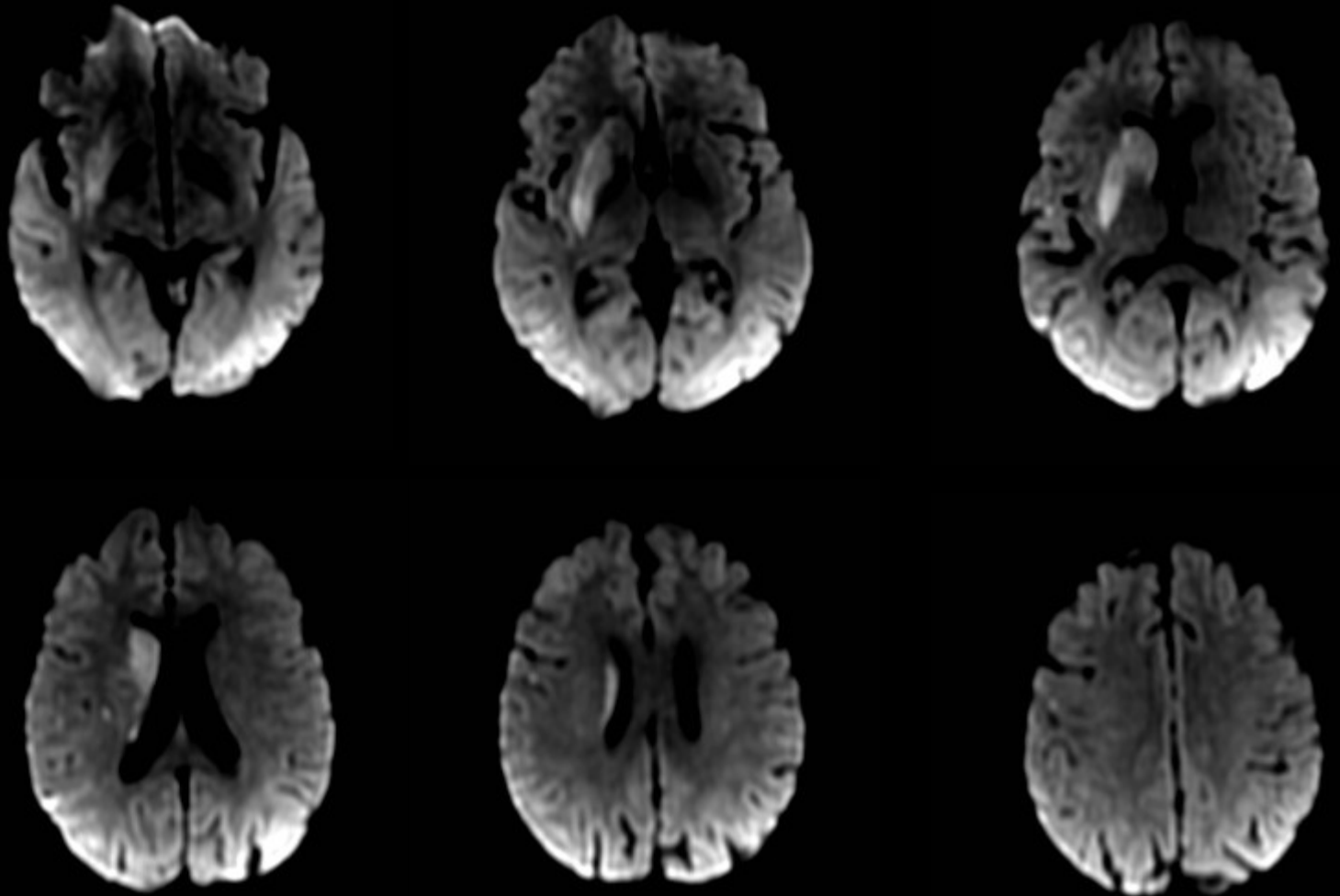
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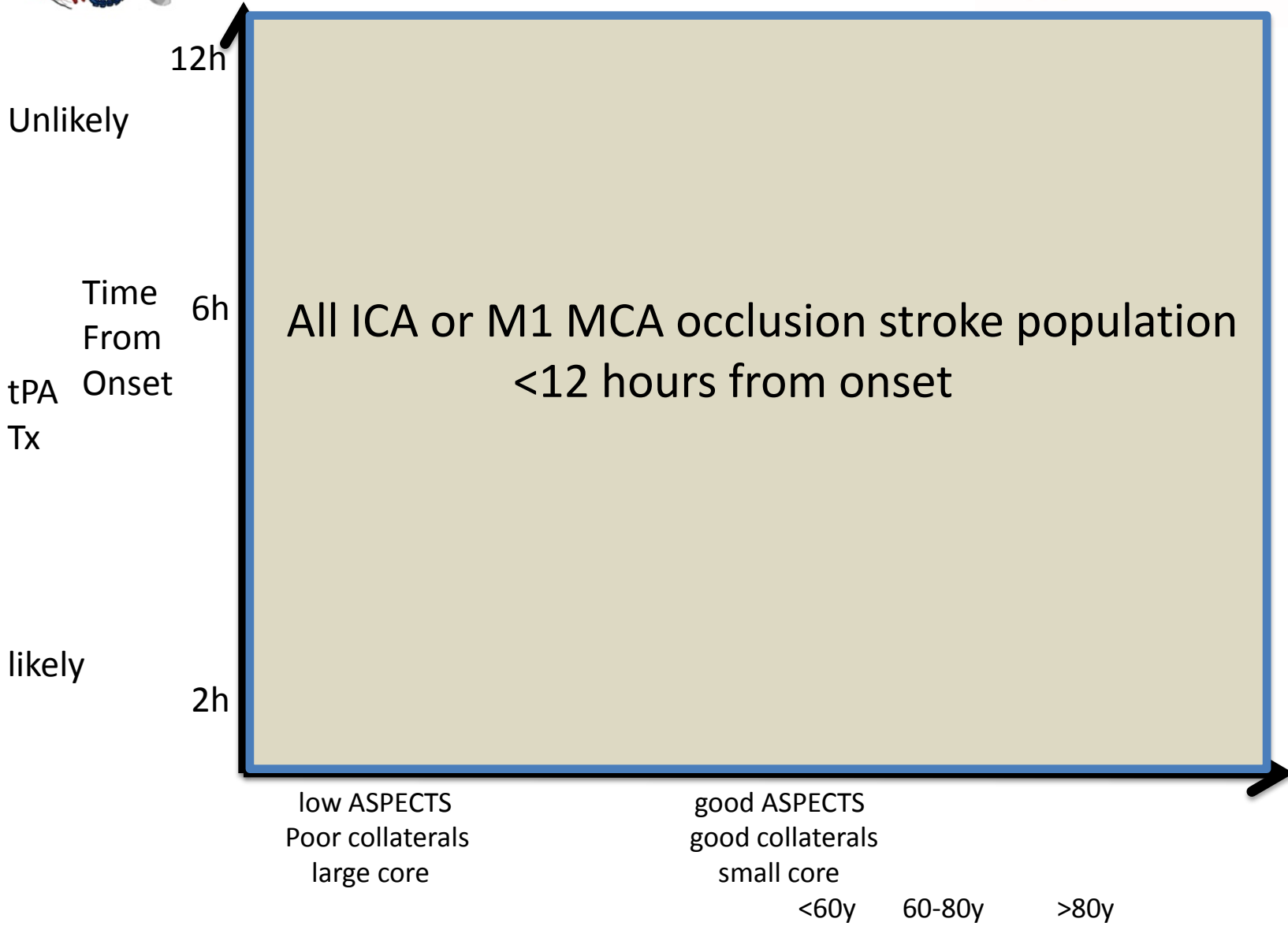


NIH down to 3



24 hour diffusion imaging
NIHSS zero
Discharged home on day 3

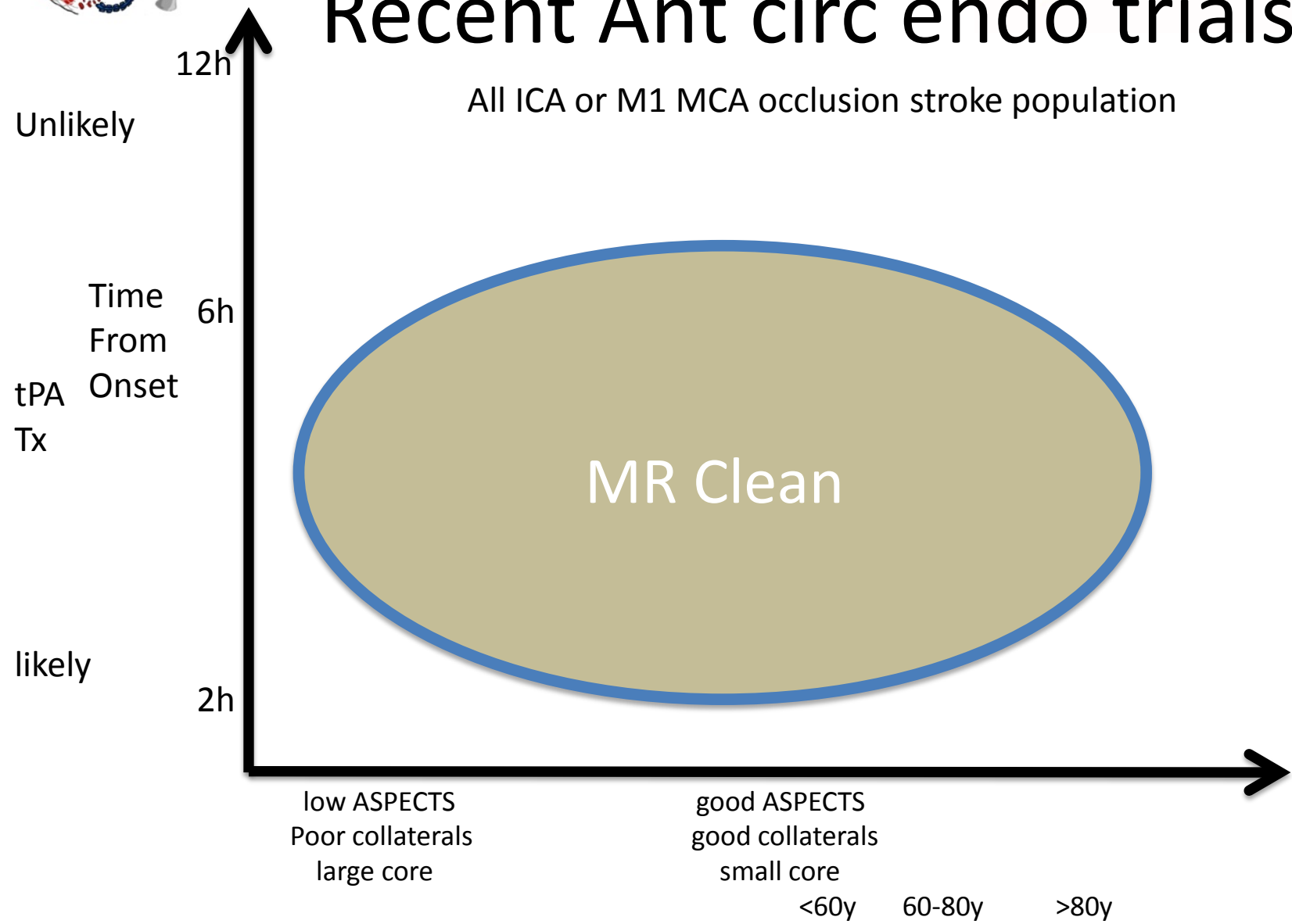






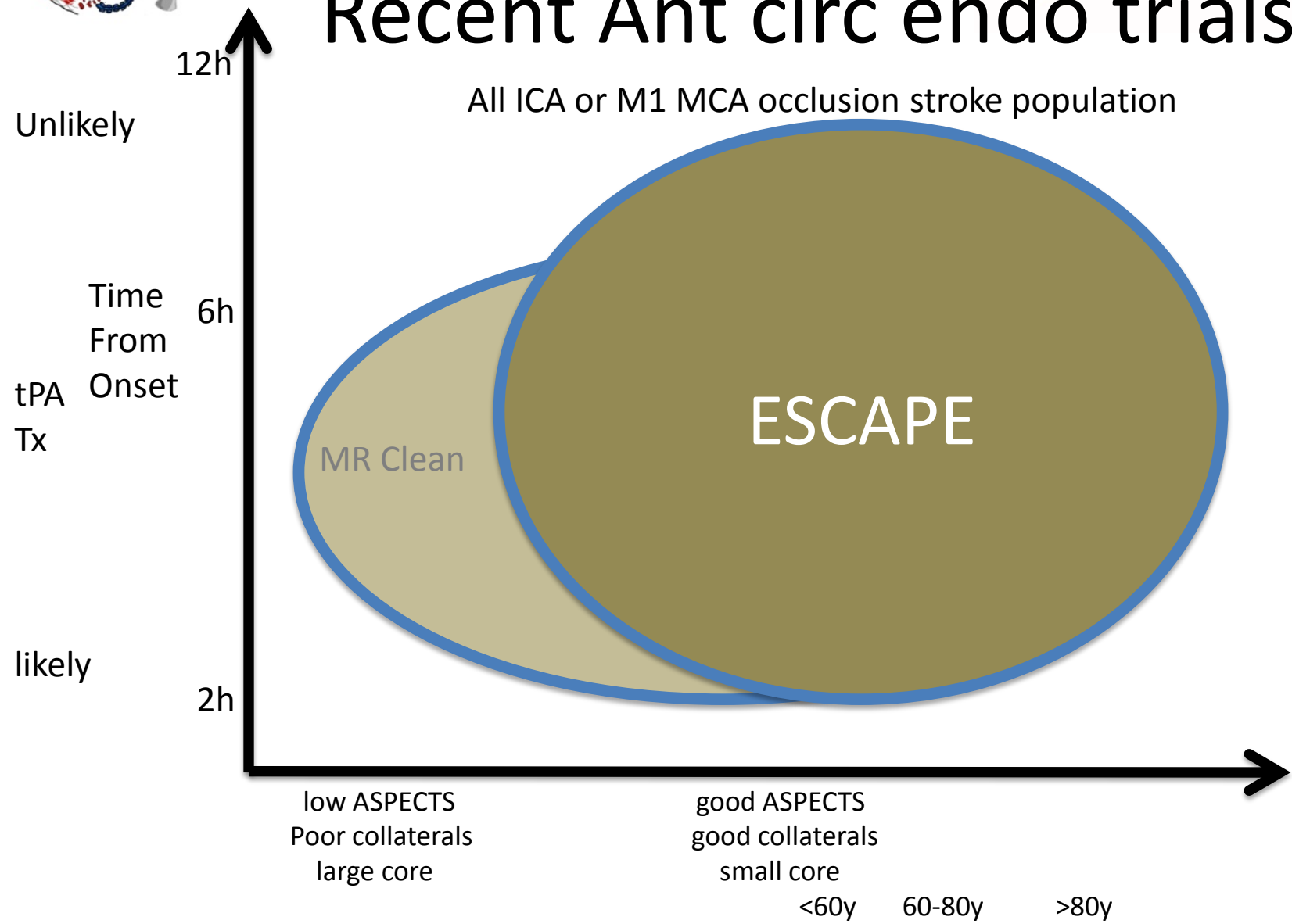
Recent Ant circ endo trials

All ICA or M1 MCA occlusion stroke population



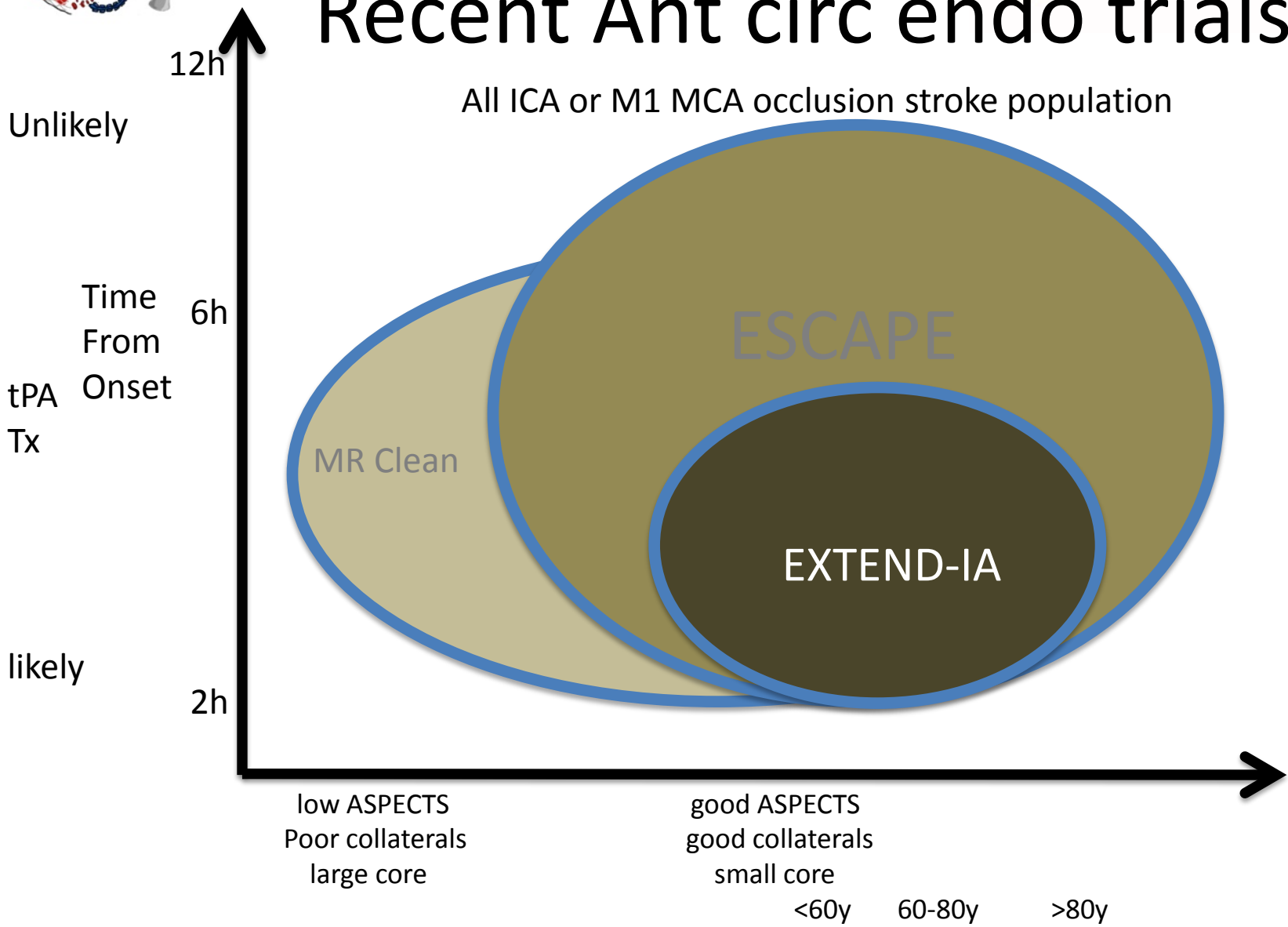


Recent Ant circ endo trials



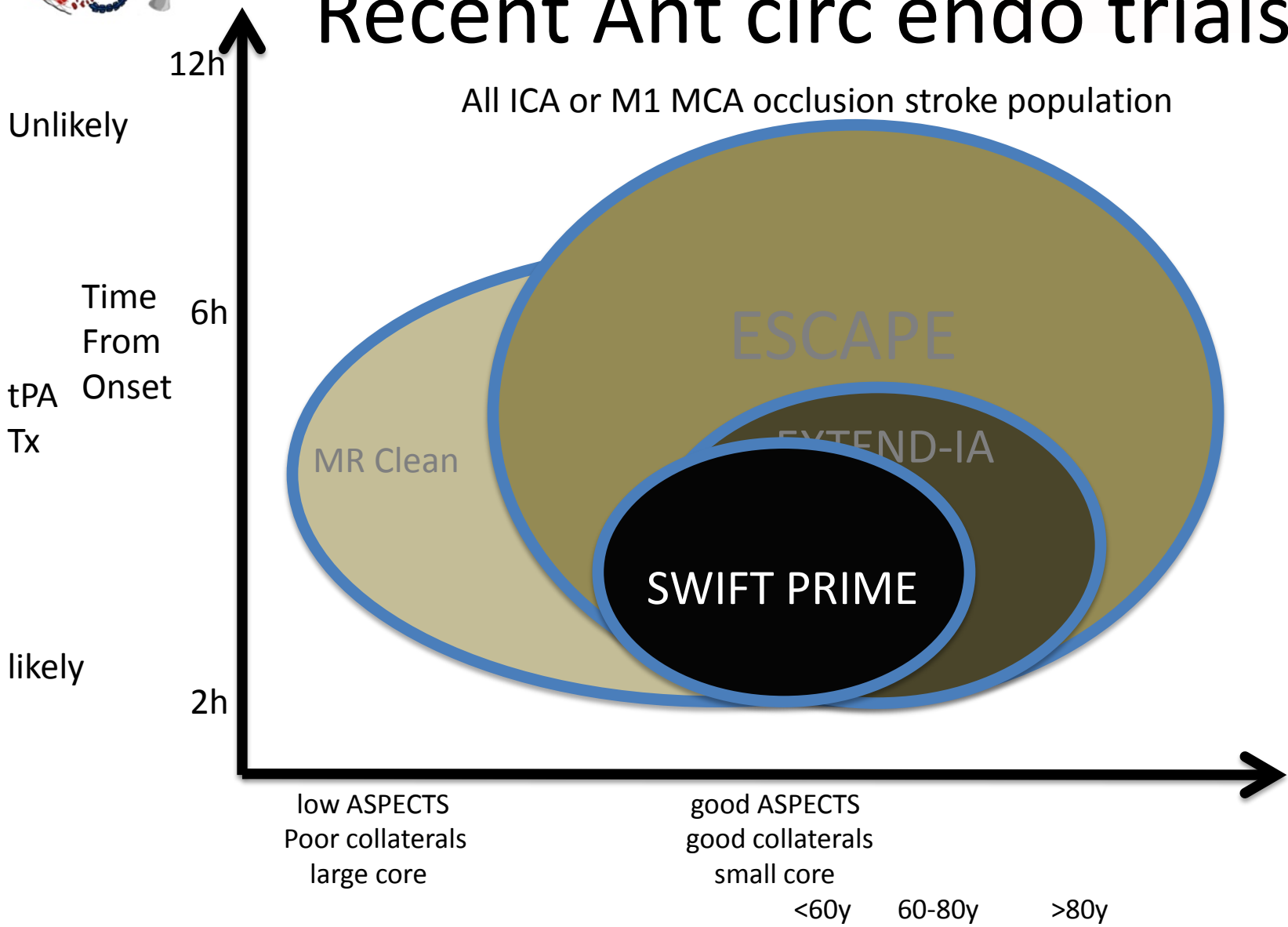


Recent Ant circ endo trials



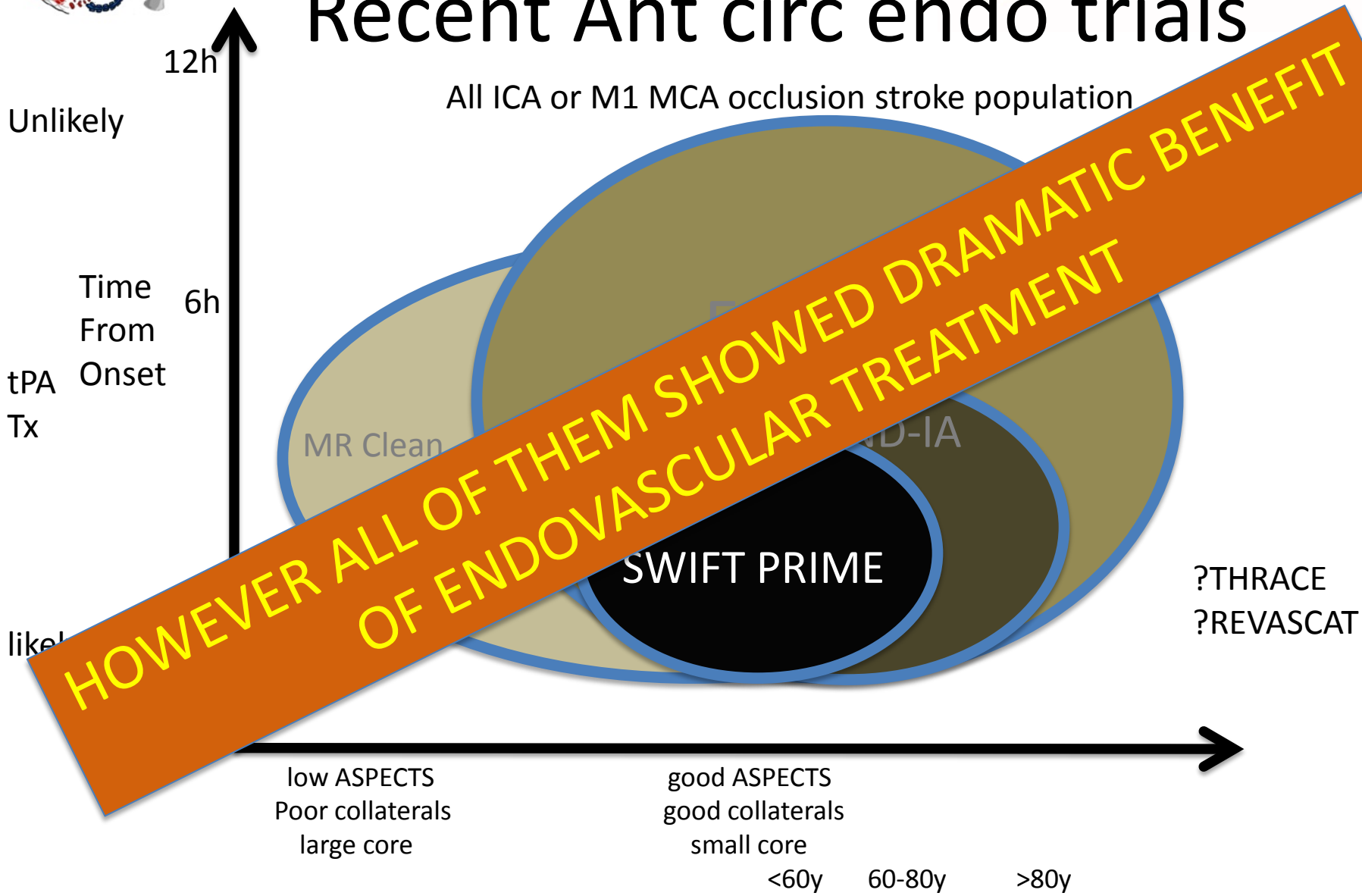


Recent Ant circ endo trials



Recent Ant circ endo trials

All ICA or M1 MCA occlusion stroke population



Conclusion

- Endovascular thrombectomy is a safe, highly effective procedure that saves lives and dramatically reduces disability WHEN:
 - Patients are carefully selected by imaging to identify proximal occlusions, and exclude large core and exclude patients with absent collaterals
 - Treatment is extremely fast with target first slice
 - imaging → to groin puncture < 60 min and
 - imaging → to reperfusion < 90 min
 - Safe effective technology (retrievable stents) is used

ESCAPE: Key Messages

- Select patients with imaging – measure the physiology - www.aspectsinstroke.com
 - Good scan (exclude the large core patients), proximal artery occlusion, moderate-good collaterals on mCTA
- Act very fast on that information
 - Picture-to-puncture (First slice CT→groin puncture) < 60 minutes
 - Picture-to-perfusion (First slice CT→reperfusion) < 90 minutes
- Achieve reperfusion – TICI 2b/3
- Work as a team!

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

M. Goyal, A.M. Demchuk, B.K. Menon, M. Eesa, J.L. Rempel, J. Thornton, D. Roy, T.G. Jovin, R.A. Willinsky, B.L. Sapkota, D. Dowlatshahi, D.F. Frei, N.R. Kamal, W.J. Montanera, A.Y. Poppe, K.J. Ryckborst, F.L. Silver, A. Shuaib, D. Tampieri, D. Williams, O.Y. Bang, B.W. Baxter, P.A. Burns, H. Choe, J.-H. Heo, C.A. Holmstedt, B. Jankowitz, M. Kelly, G. Linares, J.L. Mandzia, J. Shankar, S.-I. Sohn, R.H. Swartz, P.A. Barber, S.B. Coutts, E.E. Smith, W.F. Morrish, A. Weill, S. Subramaniam, A.P. Mitha, J.H. Wong, M.W. Lowerison, T.T. Sajobi, and M.D. Hill for the ESCAPE Trial Investigators*

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CALGARY STROKE PROGRAM



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The 22 ESCAPE Site Teams



16/04/2015

www.escapetrial.org

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A clear glass bottle with a stopper, containing a yellowish-brown liquid, likely representing tPA.

tPA: GIVE THE JUICE!