

Large Ischemic Core Thrombectomy

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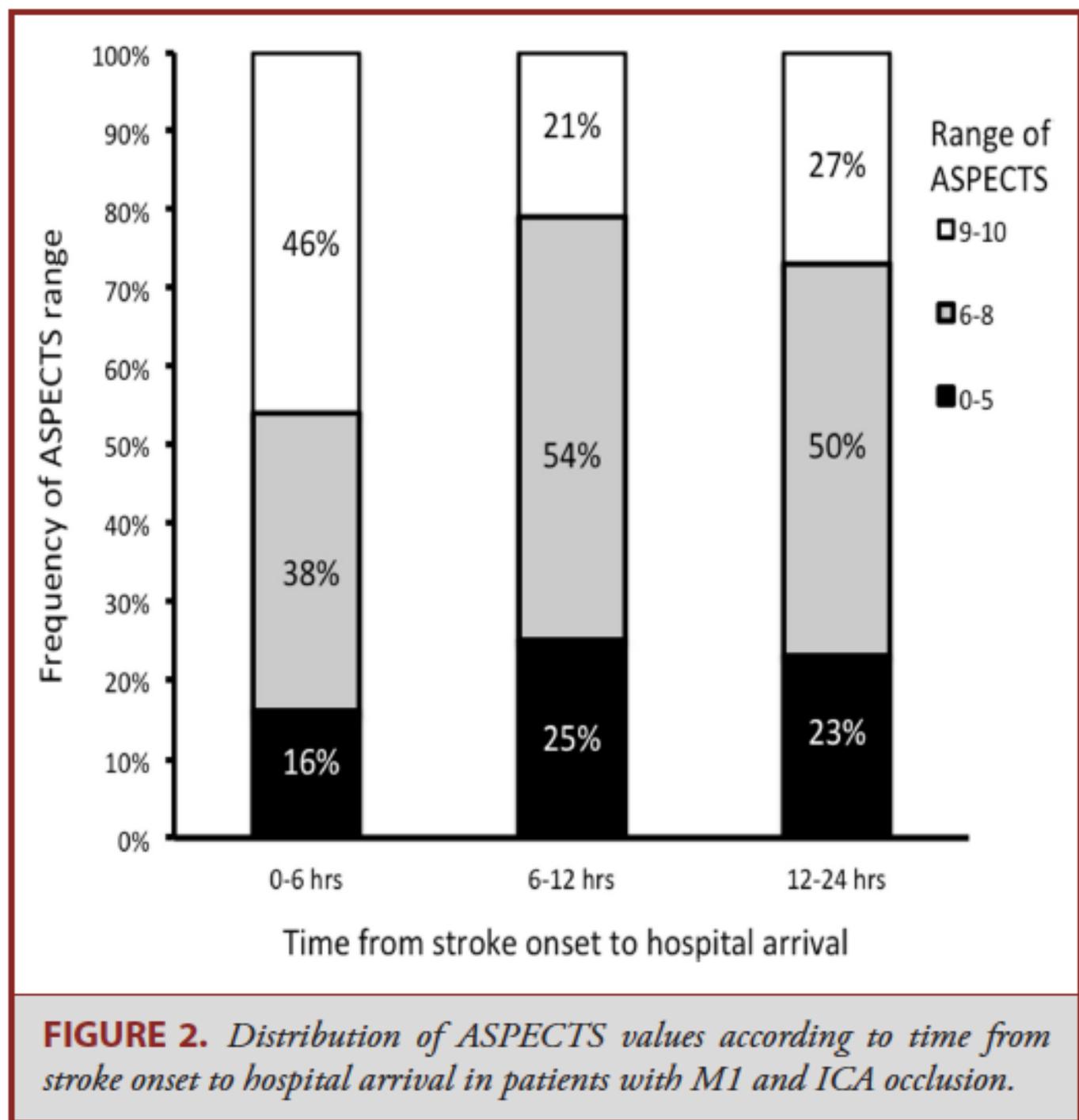


Large Ischemic Core

Patients with large stroke
comprise 1 in 5 patients with LVO

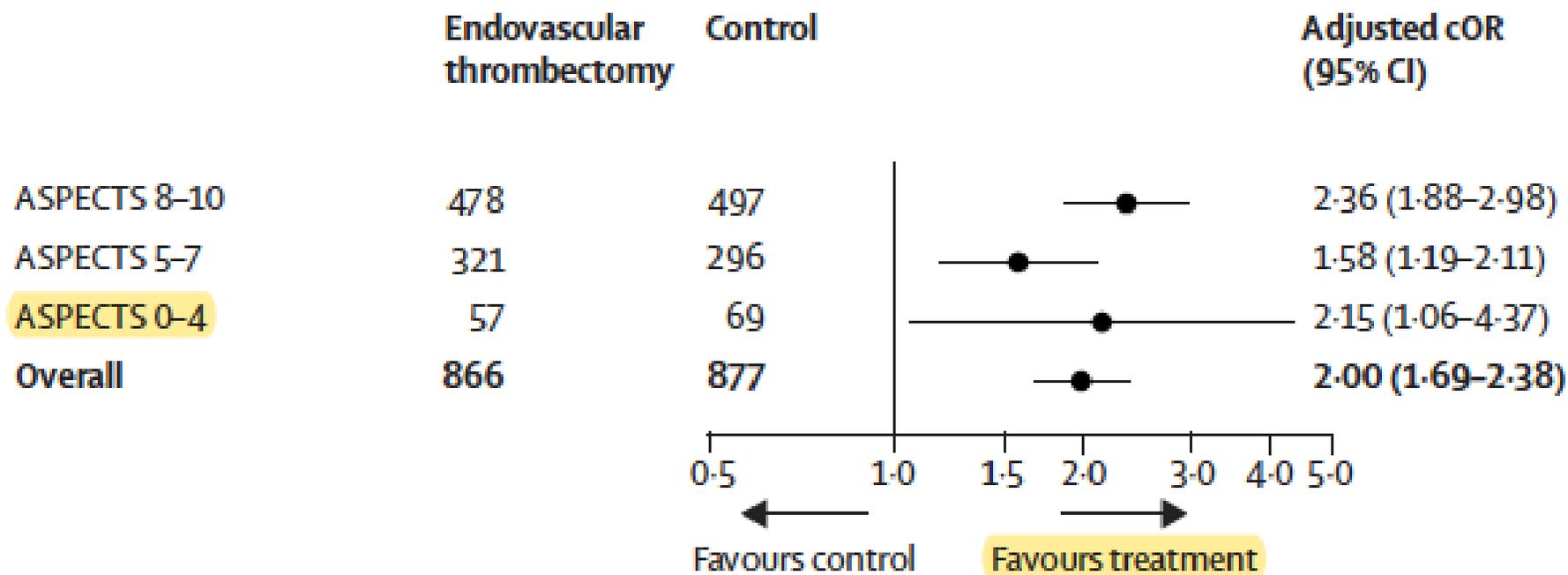
989 AIS in 2014-2015
224 LVO (1/5)

Mokin M et al. ASPECTS LVO and time of
symptom onset: Estimation of eligibility
for EVT. Neurosurgery 2017



Imaging features and safety and efficacy of endovascular stroke treatment: a meta-analysis of individual patient-level data

Luis San Román*, Bijoy K Menon*, Jordi Blasco, María Hernández-Pérez, Antoni Dávalos, Charles B L M Majoie, Bruce C V Campbell, Francis Guillemin, Hester Lingsma, René Anxionnat, Jonathan Epstein, Jeffrey L Saver, Henk Marquering, John H Wong, Demetrius Lopes, Gernot Reimann, Hubert Desal, Diederik W J Dippel, Shelagh Coutts, Richard du Mesnil de Rochemont, Dileep Yavagal, Jean Christophe Ferre, Yvo B W E M Roos, David S Liebeskind, Robert Lenthall, Carlos Molina, Fahad S Al Ajlan, Vivek Reddy, Dar Dowlathshahi, Nader-Antoine Sourour,



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Endovascular Therapy for Acute Stroke with a Large Ischemic Region

S. Yoshimura, N. Sakai, H. Yamagami, K. Uchida, M. Beppu, K. Toyoda, Y. Matsumaru, Y. Matsumoto, K. Kimura, M. Takeuchi, Y. Yazawa, N. Kimura, K. Shigeta, H. Imamura, I. Suzuki, Y. Enomoto, S. Tokunaga, K. Morita, F. Sakakibara, N. Kinjo, T. Saito, R. Ishikura, M. Inoue, and T. Morimoto

Endovascular thrombectomy for acute ischaemic stroke with established large infarct: multicentre, open-label, randomised trial

Martin Bendszus, Jens Fiehler, Fabien Subtil, Susanne Bonekamp, Anne Hege Aamodt, Blanca Fuentes, Elke R Gizewski, Michael D Hill, Antonin Krajina, Laurent Pierot, Claus Z Simonsen, Kamil Zelenák, Rolf A Blauenfeldt, Bastian Cheng, Angélique Denis, Hannes Deutschmann, Franziska Dorn, Fabian Flottmann, Susanne Gellissen, Johannes C Gerber, Mayank Goyal, Jozef Haring, Christian Herweh, Silke Hopf-Jensen, Vi Tuan Hua, Mårit Jensen, Andreas Kastrup, Christiane Fee Keil, Andrej Klepanec, Egon Kurča, Ronni Mikkelsen, Markus Möhlenbruch, Stefan Müller-Hülsbeck, Nico Münnich, Paolo Pagano, Panagiotis Papanagiotou, Gabor C Petzold, Mirko Pham, Volker Puetz, Jan Raupach, Gemot Reimann, Peter Arthur Ringleb, Maximilian Schell, Eckhard Schlemm, Silvia Schönenberger, Bjørn Tennøe, Christian Ulfert, Kateřina Valis, Eva Vitková, Dominik F Vollherbst, Wolfgang Wick, Götz Thomalla, on behalf of the TENSION Investigators*

ORIGINAL ARTICLE

Trial of Endovascular Therapy for Acute Ischemic Stroke with Large Infarct

X. Huo, G. Ma, X. Tong, X. Zhang, Y. Pan, T.N. Nguyen, G. Yuan, H. Han, W. Chen, M. Wei, JIANGANG ZHANG, Z. Zhou, X. Yao, G. Wang, W. Song, X. Cai, G. Nan, D. Li, A.Y.-C. Wang, W. Ling, C. Cai, C. Wen, E. Wang, L. Zhang, C. Jiang, Y. Liu, G. Liao, X. Chen, T. Li, S. Liu, J. Li, F. Gao, N. Ma, D. Mo, L. Song, X. Sun, X. Li, Y. Deng, G. Luo, M. Lv, H. He, A. Liu, JINGBO ZHANG, S. Mu, Lian Liu, J. Jing, X. Nie, Z. Ding, W. Du, X. Zhao, P. Yang, Liping Liu, Yilong Wang, D.S. Liebeskind, V.M. Pereira, Z. Ren, Yongjun Wang, and Z. Miao, for the ANGEL-ASPECT Investigators*

ORIGINAL ARTICLE

Trial of Thrombectomy for Stroke with a Large Infarct of Unrestricted Size

V. Costalat, T.G. Jovin, J.F. Albuher, C. Cognard, H. Henon, N. Nouri, B. Gory, S. Richard, G. Marnat, I. Sibon, F. Di Maria, M. Annan, G. Boulouis, P. Cardona, M. Obadia, M. Piotin, R. Bourcier, B. Guillon, S. Godard, A. Pasco-Papon, O.F. Eker, T.-H. Cho, G. Turc, O. Naggara, S. Velasco, M. Lamy, F. Clarençon, S. Alamowitch, A. Renu, L. Suissa, H. Brunel, J.-C. Gentic, S. Timsit, C. Lamy, C. Chivot, F. Macian-Montoro, C. Mounayer, O. Ozkul-Wermester, C. Papagiannaki, V. Wolff, R. Pop, A. Ferrier, E. Chabert, F. Ricolfi, Y. Béjot, E. Lopez-Cancio, P. Vega, L. Spelle, C. Denier, M. Millán, J.F. Arenillas, M. Mazighi, E. Houdart, M. del Mar Freijo, A. Duhamel, N. Sanossian, D.S. Liebeskind, J. Labreuche, B. Lapergue, and C. Arquizan, for the LASTE Trial Investigators*

ORIGINAL ARTICLE

Trial of Endovascular Thrombectomy for Large Ischemic Strokes

A. Sarraj, A.E. Hassan, M.G. Abraham, S. Ortega-Gutierrez, S.E. Kasner, M.S. Hussain, M. Chen, S. Blackburn, C.W. Sitton, L. Churilov, S. Sundararajan, Y.C. Hu, N.A. Herial, P. Jabbour, D. Gibson, A.N. Wallace, J.F. Arenillas, J.P. Tsai, R.F. Budzik, W.J. Hicks, O. Kozak, B. Yan, D.J. Cordato, N.W. Manning, M.W. Parsons, R.A. Hanel, A.N. Aghaebrahim, T.Y. Wu, P. Cardona-Portela, N. Pérez de la Ossa, J.D. Schaafsma, J. Blasco, N. Sangha, S. Warach, C.D. Gandhi, T.J. Kleinig, D. Sahlein, L. Eljovich, W. Tekle, E.A. Samaniego, L. Maali, M.A. Abdulrazzak, M.N. Psychogios, A. Shuaib, D.K. Pujara, F. Shaker, H. Johns, G. Sharma, V. Yogendrakumar, F.C. Ng, M.H. Rahbar, C. Cai, P. Lavori, S. Hamilton, T. Nguyen, J.T. Fifi, S. Davis, L. Wechsler, V.M. Pereira, M.G. Lansberg, M.D. Hill, J.C. Grotta, M. Ribo, B.C. Campbell, and G.W. Albers, for the SELECT2 Investigators*

JAMA | [Original Investigation](#)

Thrombectomy for Stroke With Large Infarct on Noncontrast CT The TESLA Randomized Clinical Trial

The Writing Committee for the TESLA Investigators

IMPORTANCE Recent large infarct thrombectomy trials used heterogeneous imaging modalities and time windows for patient selection. Noncontrast computed tomographic (CT) scan is the most common stroke imaging approach. It remains uncertain whether thrombectomy is effective for patients with large infarcts identified using noncontrast CT alone within 24 hours of stroke onset.

The Writing Committee for the TESLA

Investigators: Albert J. Yoo, MD, PhD; Osama O. Zaidat, MD, MS; Sunil A. Sheth, MD; Ansaar T. Rai, MD; Santiago Ortega-Gutierrez, MD, MSc; Curtis A. Given II, MD; Syed F. Zaidi, MD; Ramesh Grandhi, MD; Hugo Cuellar, MD; Maxim Mokin, MD, PhD; Jeffrey M. Katz, MD; Amer Alsheklee, MD; Muhammad A. Taqi, MD; Sameer A. Ansari, MD, PhD; Adnan H. Siddiqui, MD, PhD; Nobl Barazangi, MD, PhD; Joey D. English, MD, PhD; Alberto Maud, MD; Jawad Kirmani, MD; Rishi Gupta, MD; Dileep R. Yavagal, MD; Jason Tarpley, MD; Dhruvil J. Pandya, MD; Marshall C. Cress, MD; Sushrut Dharmadhikari, MD; Kaiz S. Asif, MD; Tareq Kass-Hout, MD; Ajit S. Puri, MD; Nazli Janjua, MD; Aniel Q. Majjho, MD; Aamir Badruddin, MD; Randall C. Edgell, MD, MSPH; Dabeek Khatri, MD; Larry Moran, MD; Anmar

 Visual Abstr

 Editorial

 Supplement



Trial	RESCUE-Japan LIMIT 	ANGEL ASPECT 	SELECT 2  	TESLA 	TENSION  	LASTE  
No. patients	203	456	352	300	253	450
Onset to randomization	0-24 h	0-24 h	0-24 h	0-24h	0-12h	0-7h or negative FLAIR if unknown time
Age, years	≥18	18-80	18-85	18-85	≥18	≥18
NIHSS	≥ 10	6-30	≥ 10	≥ 6	<26	
Pre-stroke mRS	0-1	0-1	0-1	0-1	0-2	0-1
Imaging selection criteria	ASPECTS 3-5, CT or MRI (DWI) if < 6 hours LKW. (If LKW 6-24 h FLAIR used)	- ASPECTS 3-5 (LKW 0-24 h) - ASPECTS 0-2 (core 70-100ml if LKW 0-24 h) - ASPECTS >5 (LKW 6-24 h and core 70-100 ml)	ASPECTS of 3-5 (core volume ≥50 ml on CTP)	NCCT ASPECTS 2-5	NCCT or DWI ASPECTS 3-5	NCCT or MRI ASPECTS 0-5 ≥ 80yo, ASPECTS 4 or 5

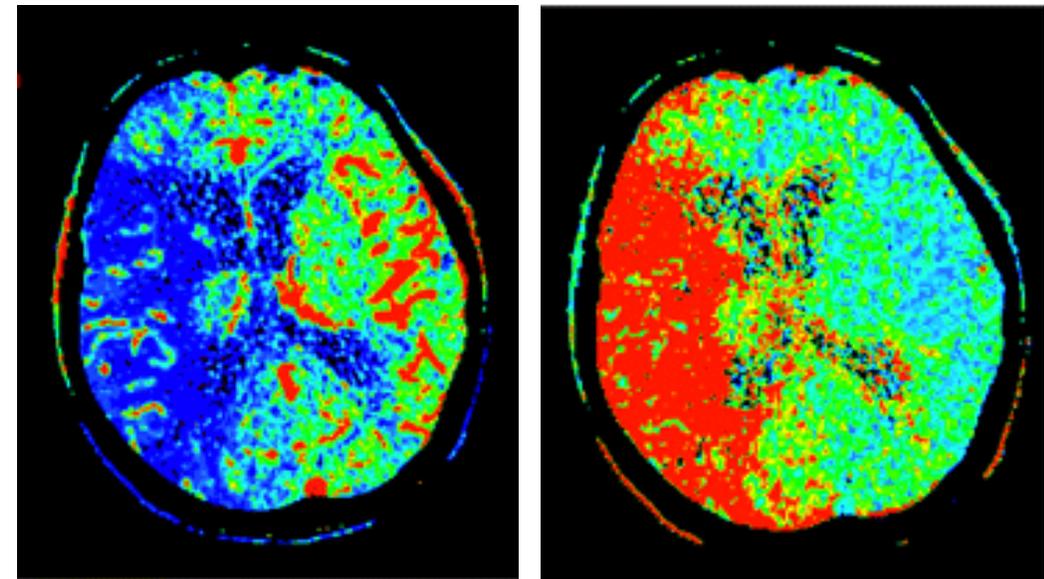
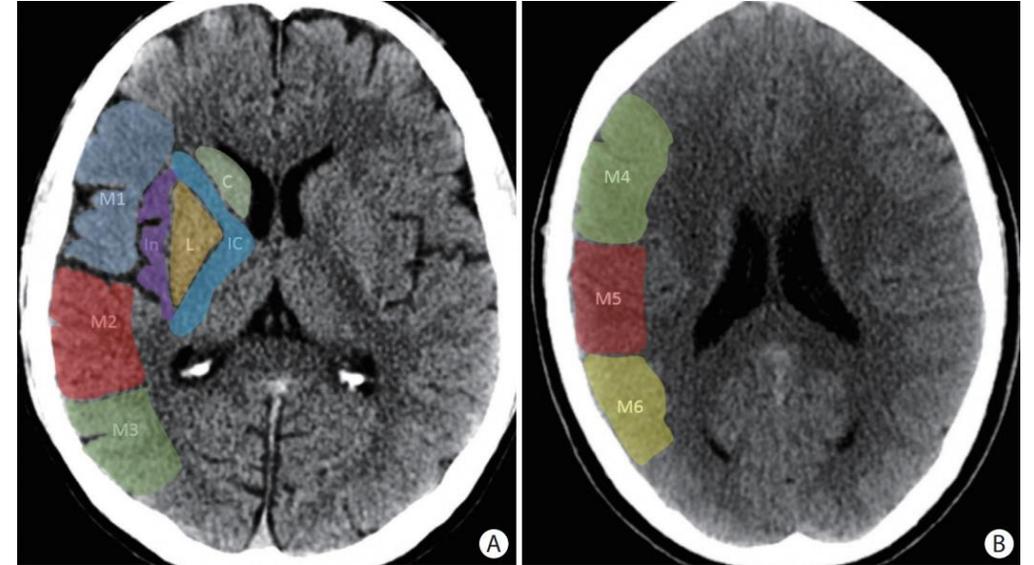
Large Core Definitions

ASPECTS: 0 to 5

- Semi-quantitative
- Lower score on MRI than CT

Ischemic core: >50ml/>70 ml

- CTP measures the volume of reduced blood flow at the time of acquisition
- MRI measures restricted diffusion / cytotoxic edema



Endovascular Thrombectomy for Large Ischemic Core Stroke

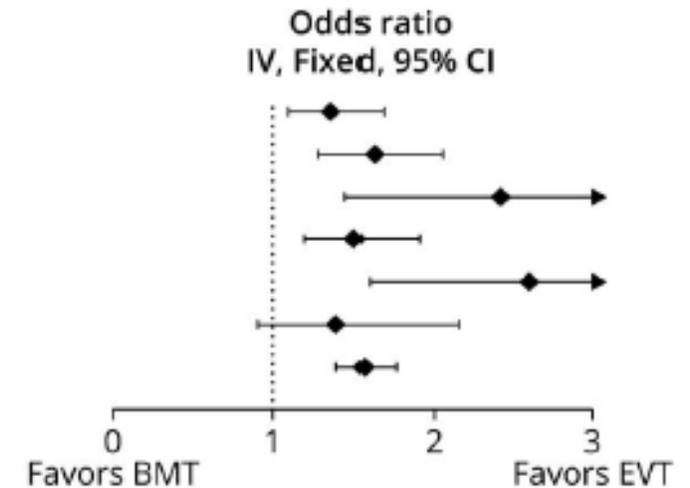
A Systematic Review and Meta-Analysis of Randomized Controlled Trials

A

Score on the modified rankin scale at 90 days

Study	LogOR	SE	Weight (%)	Odds ratio IV, Fixed, 95% CI
ANGEL-ASPECT	0.31	0.11	30.6	1.4 (1.1, 1.7)
LASTE	0.49	0.12	24.7	1.6 (1.3, 2.1)
RESCUE-Japan LIMIT	0.88	0.26	5.3	2.4 (1.5, 4.0)
SELECT2	0.41	0.12	26.2	1.5 (1.2, 1.9)
TENSION	0.95	0.24	6.0	2.6 (1.6, 4.2)
TESLA	0.34	0.22	7.2	1.4 (0.9, 2.2)
Total (95% CI)			100.0	1.6 (1.4, 1.8)

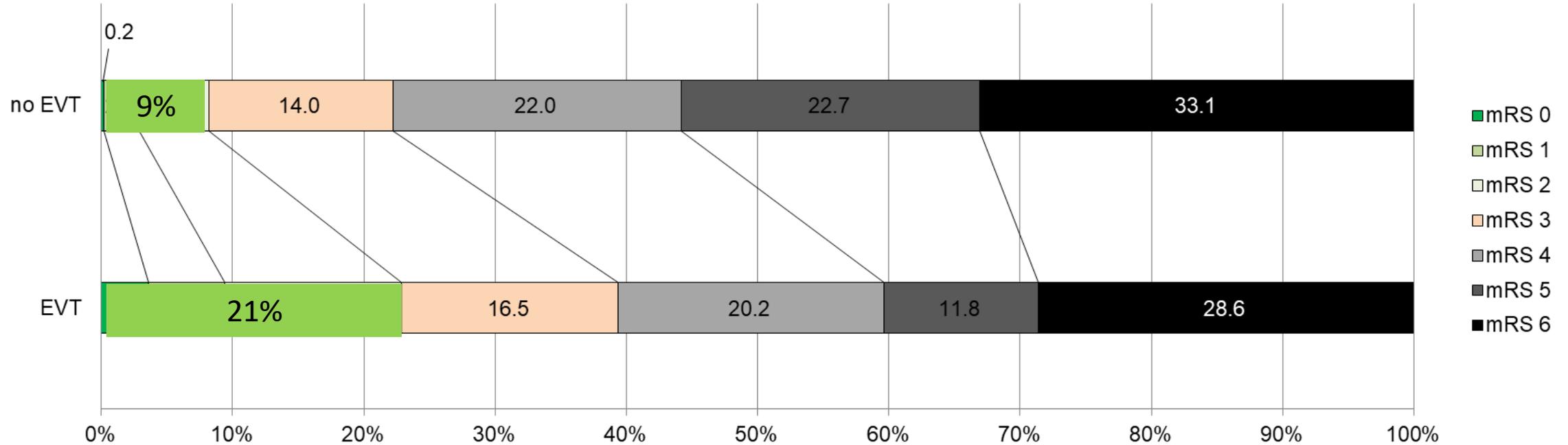
Heterogeneity: $\text{Tau}^2 = 0.019$; $\text{Chi}^2 = 9.09$, $\text{df} = 5$ ($p = 0.11$); $I^2 = 45\%$
Test for overall effect: $z = 7.63$ ($p < 0.01$)



90-day mRS: EVT vs BMT, OR 1.6 [95% CI 1.4, 1.8]

Mechanical Thrombectomy in Ischemic Stroke with a Infarct Core: A Meta-Analysis of Randomized Contro

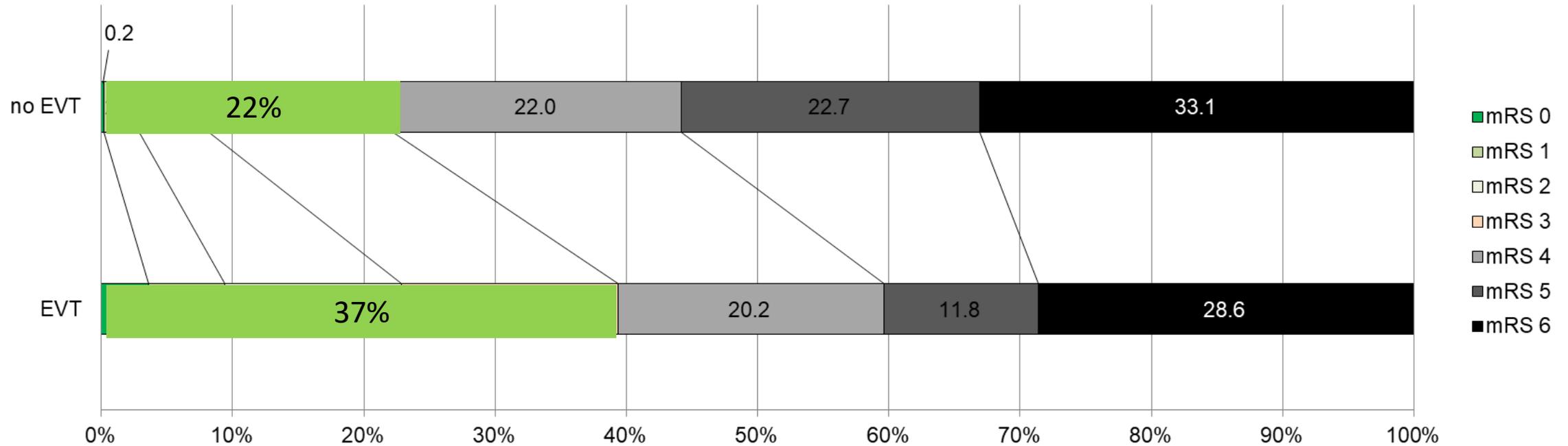
Michele Romoli ^{1,*}, Lucia Princiotta Cariddi ², Marco Longoni ^{1,†}, Gianluca Stufano ¹, Sebastiano Giacomozzi ¹, Luca Pompei ², Francesco Diana ^{3,†}, Lucio D'Anna ^{4,5,†}, Simona Sacco ^{6,†} and Simone Vidale ^{2,†}



90-day mRS 0-2: OR 2.47, 95%CI 1.5–4.0, p<0.001

Mechanical Thrombectomy in Ischemic Stroke with a Infarct Core: A Meta-Analysis of Randomized Contro

Michele Romoli ^{1,*}, Lucia Princiotta Cariddi ², Marco Longoni ^{1,†}, Gianluca Stufano ¹, Sebastiano Giacomozzi ¹, Luca Pompei ², Francesco Diana ^{3,†}, Lucio D'Anna ^{4,5,†}, Simona Sacco ^{6,†} and Simone Vidale ^{2,†}



90-day mRS 0-3: OR 2.20, 95%CI 1.7–2.8, p<0.001 (5 RCTs)

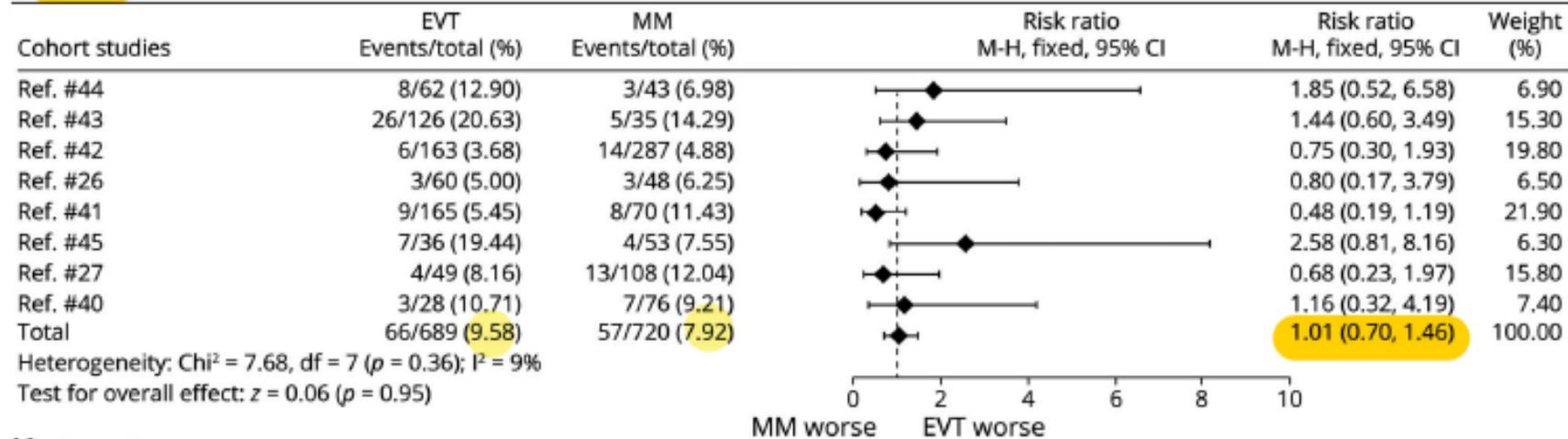
Symptomatic ICH in Large Ischemic Core

6 Randomized trials Meta-analysis, Symptomatic ICH Risk: **5.5%** vs. 3.2%

RR 1.71 [95% CI, 1.09–2.66]

Real-Life, Observational Meta-analysis, Symptomatic ICH Risk: **9.6%** vs. 7.9%

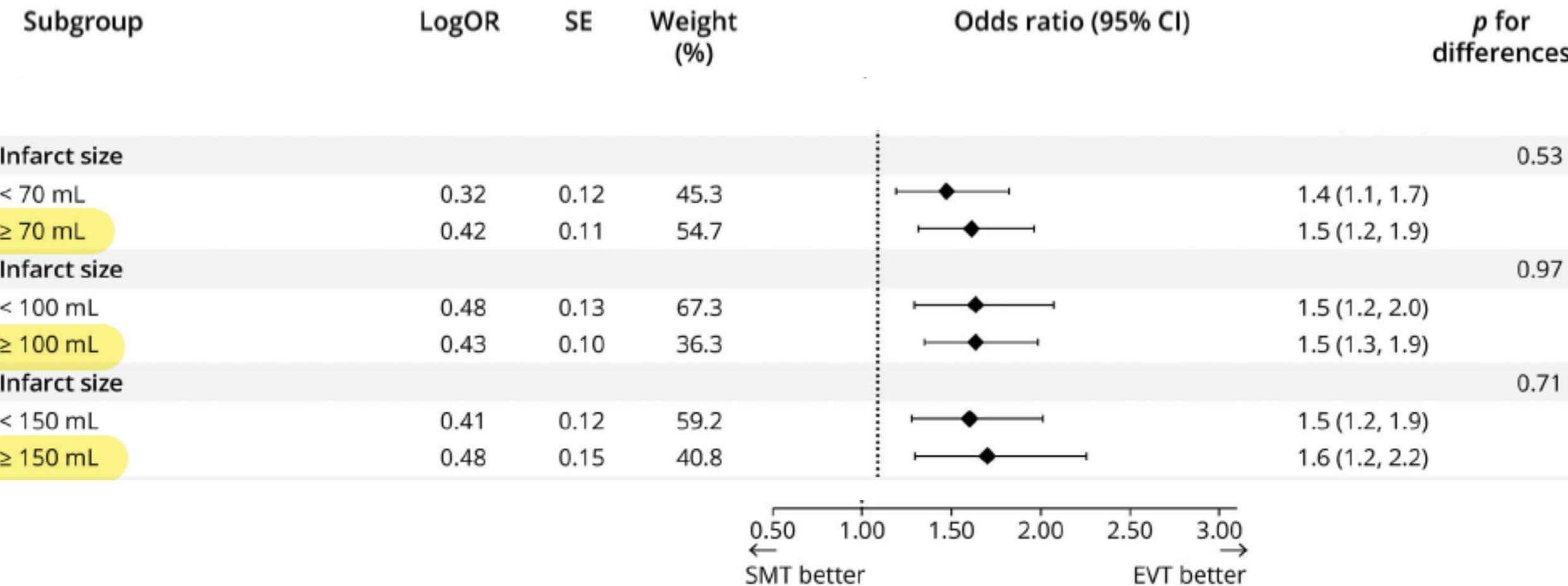
C. sICH



Does size of the infarct matter?

Endovascular Thrombectomy for Large Ischemic Core Stroke

A Systematic Review and Meta-Analysis of Randomized Controlled Trials



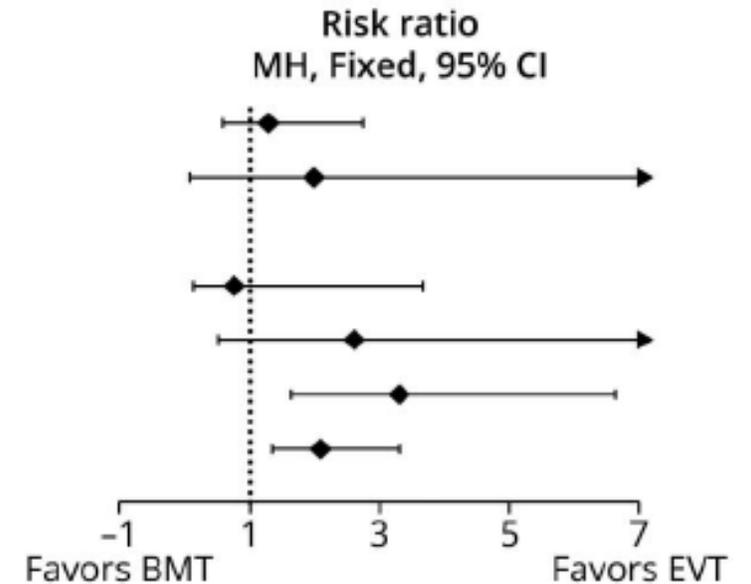
ASPECTS 0 to 2 subgroup (6 trials)

A

90-Day mRS 0-3

Study	EVT Events/Total (%)	BMT Events/Total (%)	Weight (%)	Risk ratio MH, Fixed, 95% CI
ANGEL-ASPECT	11/32 (34.37)	8/30 (26.67)	37.0	1.3 (0.6, 2.8)
RESCUE-Japan LIMIT	1/5 (20.00)	0/3 (0.00)	2.7	2.0 (0.1, 37.8)
SELECT2	0/12 (0.00)	0/8 (0.00)	0.0	
TENSION	2/15 (13.33)	4/23 (17.39)	14.2	0.8 (0.2, 3.7)
TESLA	4/22 (18.18)	2/29 (6.90)	7.7	2.6 (0.5, 13.1)
LASTE	27/86 (31.40)	9/95 (9.47)	38.4	3.3 (1.7, 6.6)
Total (95% CI)	45/172 (26.16)	23/188 (12.23)	37.0	2.1 (1.4, 3.3)

Heterogeneity: $\text{Tau}^2 = 0.076$; $\text{Chi}^2 = 4.90$, $\text{df} = 4$ ($p = 0.30$); $I^2 = 18\%$
 Test for overall effect: $z = 3.26$ ($p < 0.01$)

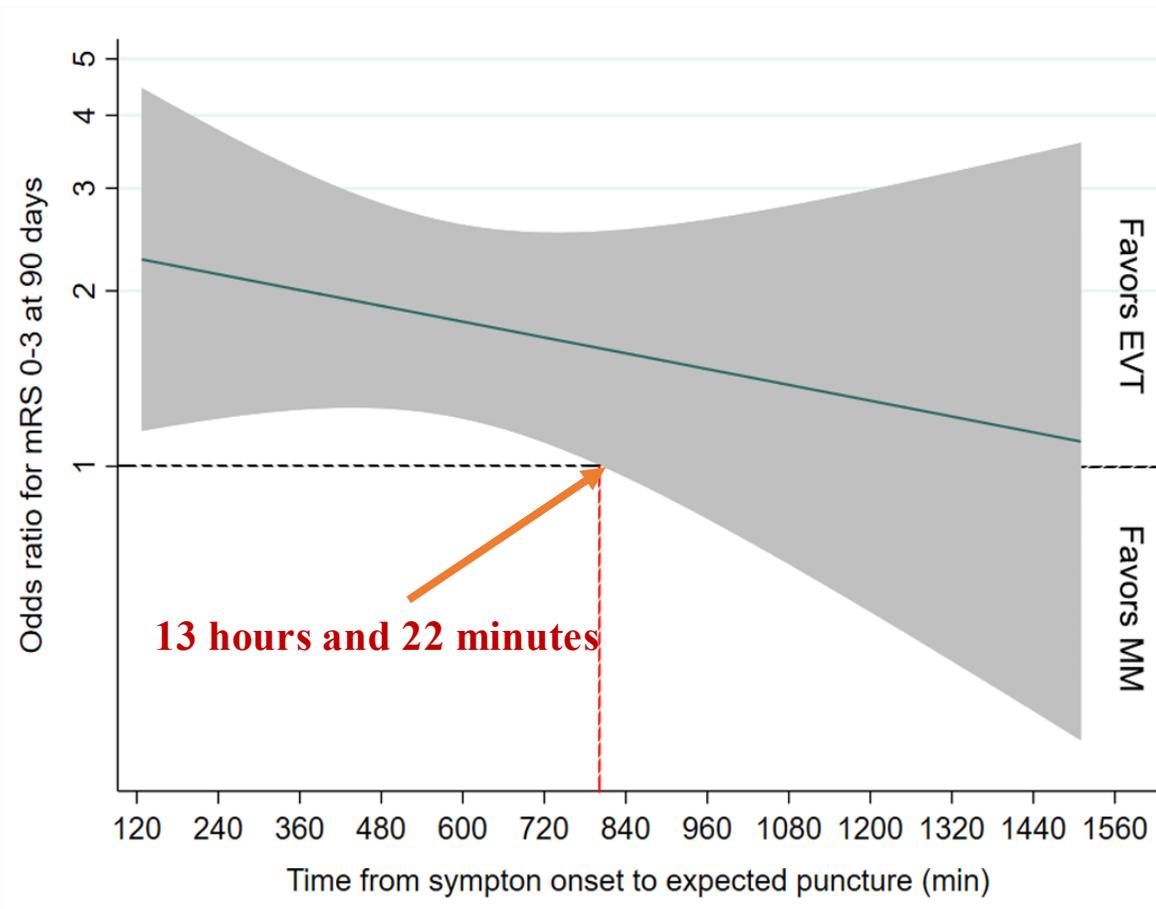


Does time to treatment matter?

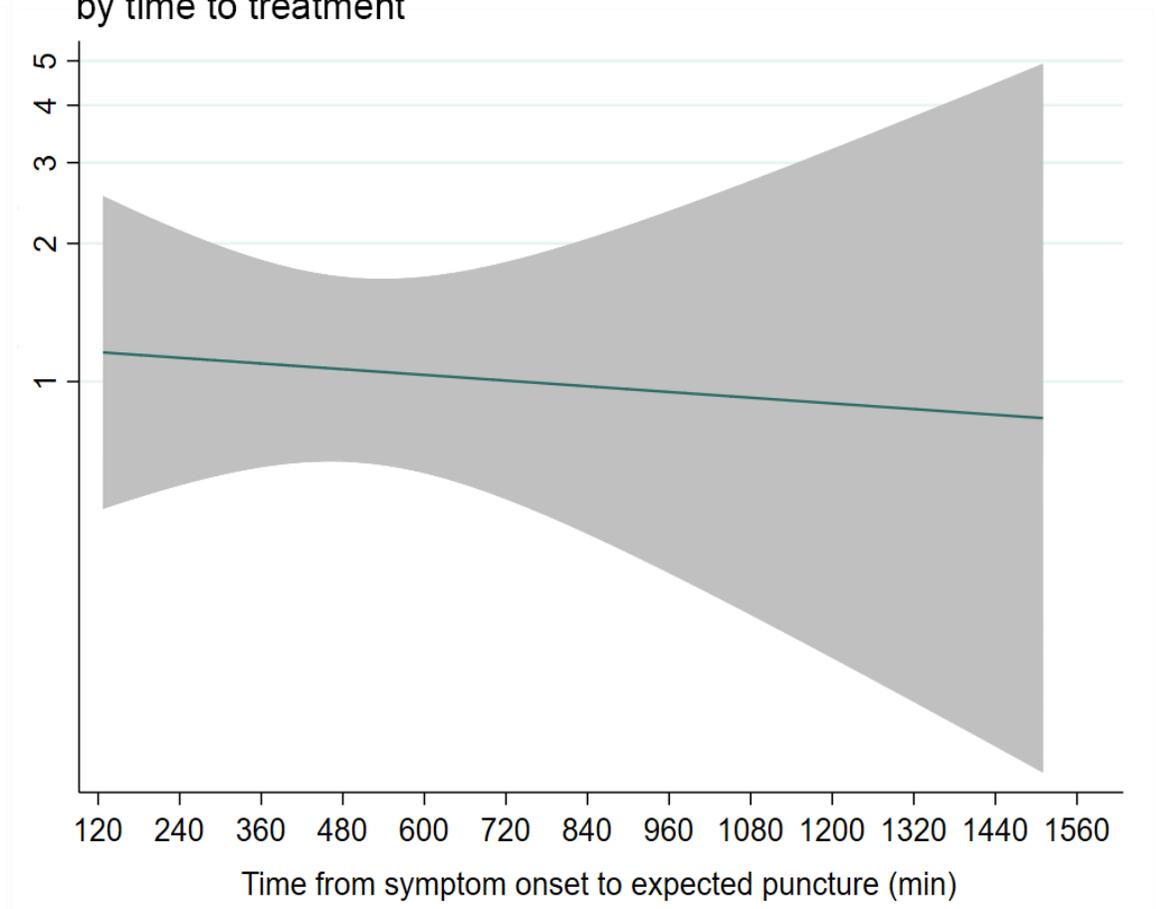
Subgroup	No. of Patients	Generalized Odds Ratio (95% CI)
Interval between time that patient was last known to be well and randomization		
<12 hr	211	1.48 (1.12–1.96)
≥12 hr	141	1.58 (1.09–2.28)
<6 hr	100	1.63 (1.09–2.46)
≥6 hr	252	1.49 (1.14–1.94)

ANGEL ASPECT

(A) Odds ratio for mRS 0-3 at 90 days in EVT vs MM groups



(B) Odds ratio for mortality at 90 days in EVT vs MM groups by time to treatment



The lower 95% CI for estimated treatment benefit crossed 1 at 13 h 22 minutes, but the point estimate exceeded 1.0 throughout the 24h period and time-benefit interaction P value was 0.38.

TESLA Post Hoc:

0- to 6-hour window

90-day mRS 0-2: **EVT 27%**(11/41) vs **MM 5%** (2/39; absolute diff., 22%; 95%CI, 5.5% to 37%).

90-day mRS 0-3: **EVT 39%** (16/41) vs **MM 18%**(7/39; absolute diff., 21%; 95%CI, 1.2% to 39%)

Mortality 90 days: EVT 22% (9/41) vs MM 38%(15/39; absolute diff., -17%; 95%CI, -35%to 3.5%) NS

6- to 24-hour window

90-day mRS 0-2: EVT 10% (11/110) vs MM 10% (11/107); absolute diff., -0.3%; 95%CI, -8.7%to8.0%);

90-day mRS 0-3: **EVT 26%** (29/110) vs **MM 21%** (22/107); absolute diff., 5.8%; 95% CI, -5.5% to 17%)

Mortality at 90 days EVT 40% (44/110) vs 32% (34/107); absolute diff., 8.2%; 95% CI, -4.5% to 21%)

Does Penumbra - Core mismatch matter?

Definition 1: N=161

Mismatch Ratio	Penumbra (Tmax > 6s)/Core volume	1.8
Mismatch Volume	Penumbra (Tmax>6s) - Core volume	15 ml

Definition 2: N=43

Mismatch Ratio	Penumbra (Tmax > 6s)/Core volume	1.2
Mismatch Volume	Penumbra (Tmax>6s) - Core volume	10 ml

JAMA | Original Investigation

Endovascular Thrombectomy for Large Ischemic Stroke Across Ischemic Injury and Penumbra Profiles

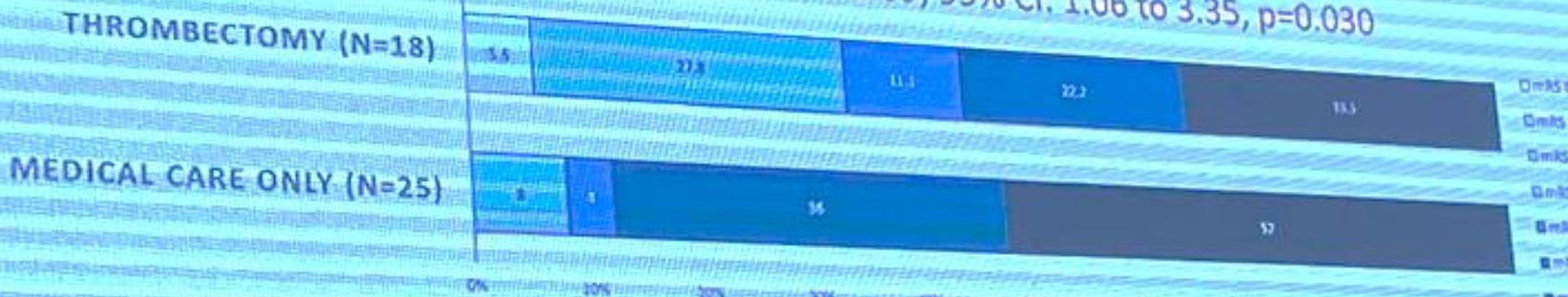
Amrou Sarraj, MD; Ameer E. Hassan, DO; Michael G. Abraham, MD; Santiago Ortega-Gutierrez, MD; Scott E. Kasner, MD; Muhammad Shazam Hussain, MD; Michael Chen, MD; Leonid Churilov, PhD; Hannah Johns, PhD; Clark W. Sifton, MD; Vignan Yogendrakumar, MD; Felix C. Ng, PhD; Deep K. Pujara, MBBS; Spiros Blackburn, MD; Sophia Sundararajan, MD; Yin C. Hu, MD; Nabeel A. Herial, MD; Juan F. Arenillas, MD, PhD; Jenny P. Tsai, MD; Ronald F. Budzik, MD; William J. Hicks, MD; Osman Kozak, MD; Bernard Yan, MBBS; Dennis J. Cordato, PhD; Nathan W. Manning, MBBS; Mark W. Parsons, PhD; Andrew Cheung, MBBS; Ricardo A. Hanel, MD; Amin N. Aghaebrahim, MD; Teddy Y. Wu, PhD; Pere Cardona Portela, MD; Chirag D. Gandhi, MD; Fawaz Al-Mufti, MD; Natalia Pérez de la Ossa, MD, PhD; Joanna D. Schaafsma, MD, PhD; Jordi Blasco, MD, PhD; Navdeep Sangha, MD; Steven Warach, MD; Timothy J. Kleinig, PhD; Faris Shaker, MBChB; Faisal Al Shaibi, MD; Gabor Toth, MD; Mohammad A. Abdulrazzak, MD; Gagan Sharma, MS; Abhishek Ray, MD; Jeffrey Sunshine, MD, PhD; Amanda Opaskar, MD; Kelsey R. Duncan, MD; Wei Xiong, MD; Edgar A. Samaniego, MD; Laith Maali, MD; Colleen G. Lechtenberg, MD; Arturo Renú, MD; Nirav Vora, MD; Thanh Nguyen, MD; Johanna T. Fifi, MD; Stavropoula I. Tjoumakaris, MD; Pascal Jabbour, MD; Georgios Tsivgoulis, MD; Vitor Mendes Pereira, MD; Maarten G. Lansberg, MD; Michael DeGeorgia, MD; Cathy A. Sila, MD; Nicholas Bambakidis, MD; Michael D. Hill, MD; Stephen M. Davis, MD; Lawrence Wechsler, MD; James C. Grotta, MD; Marc Ribo, MD; Greg W. Albers, MD; Bruce C. Campbell, PhD; for the SELECT2 Investigators

Association of Mismatch Profiles and Clinical Outcome from Endovascular Therapy in Large Infarct: A Post-Hoc Analysis of the ANGEL-ASPECT Trial

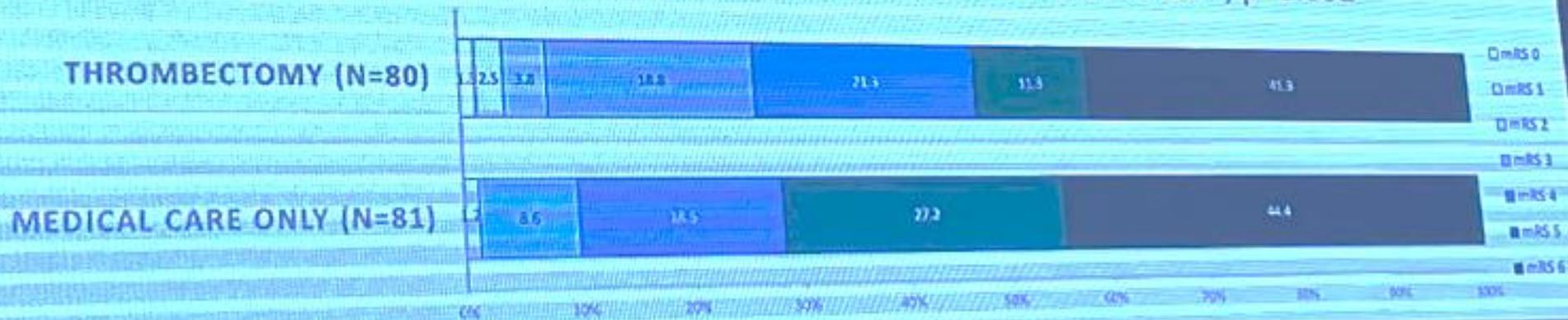
Xiaochuan Huo, MD,¹ Thanh N Nguyen, MD,² Dapeng Sun, MD, PhD ,^{3,4} Raynald, MD,³ Yuesong Pan, PhD ,^{3,4} Gaoting Ma, MD,⁵ Xu Tong, MD,³ Mengxing Wang, PhD ,⁴ Ning Ma, MD ,^{3,4} Feng Gao, MD,^{3,4} Dapeng Mo, MD ,^{3,4} Mohamad Abdalkader, MD,² Hesham E. Masoud, MD,⁶ Raul G. Nogueira, MD,⁷ and Zhongrong Miao, MD,^{3,4}
for the ANGEL-ASPECT study group

Patients without Mismatch & core ≥ 70 ml SELECT2 + ANGEL ASPECT

No Mismatch (1.2/10); aGenOR: 1.89, 95% CI: 1.06 to 3.35, p=0.030

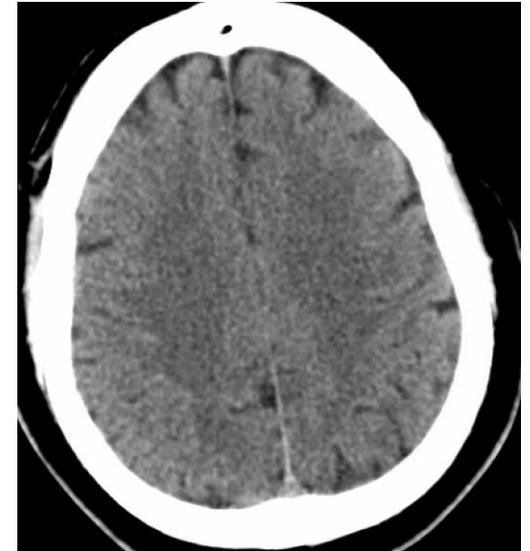
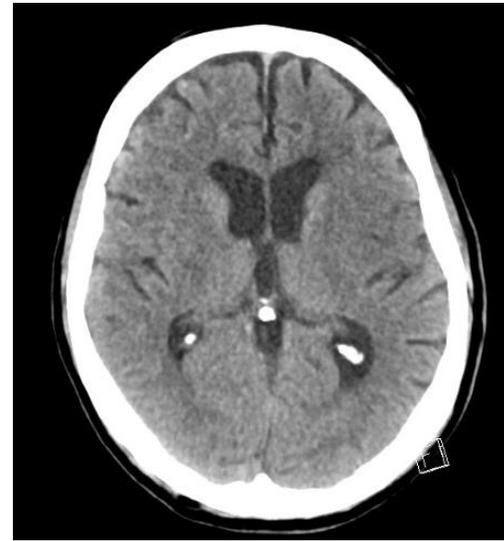
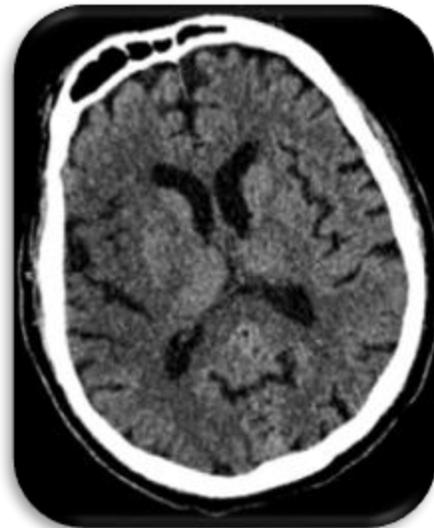
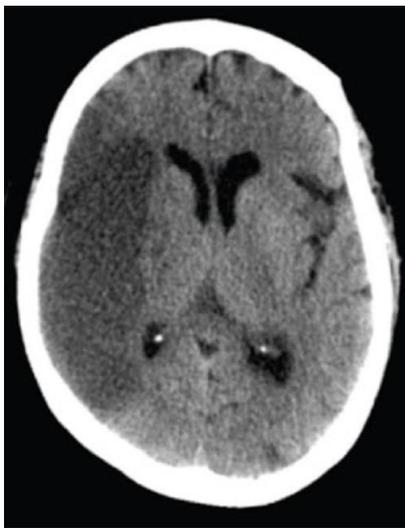
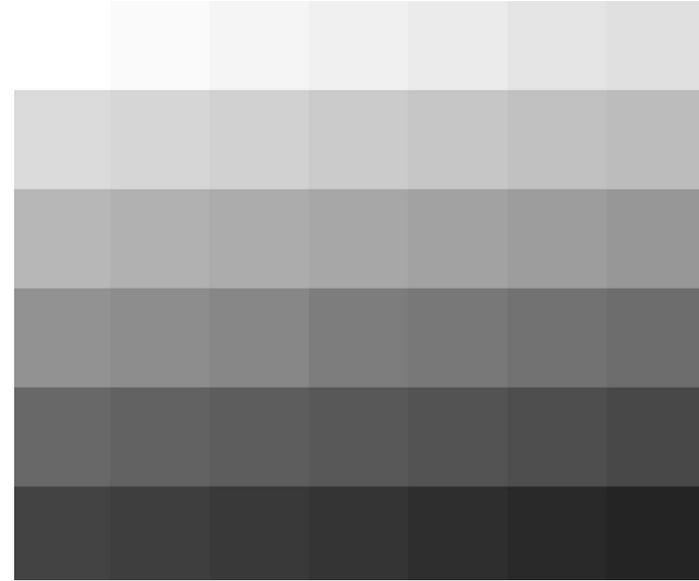


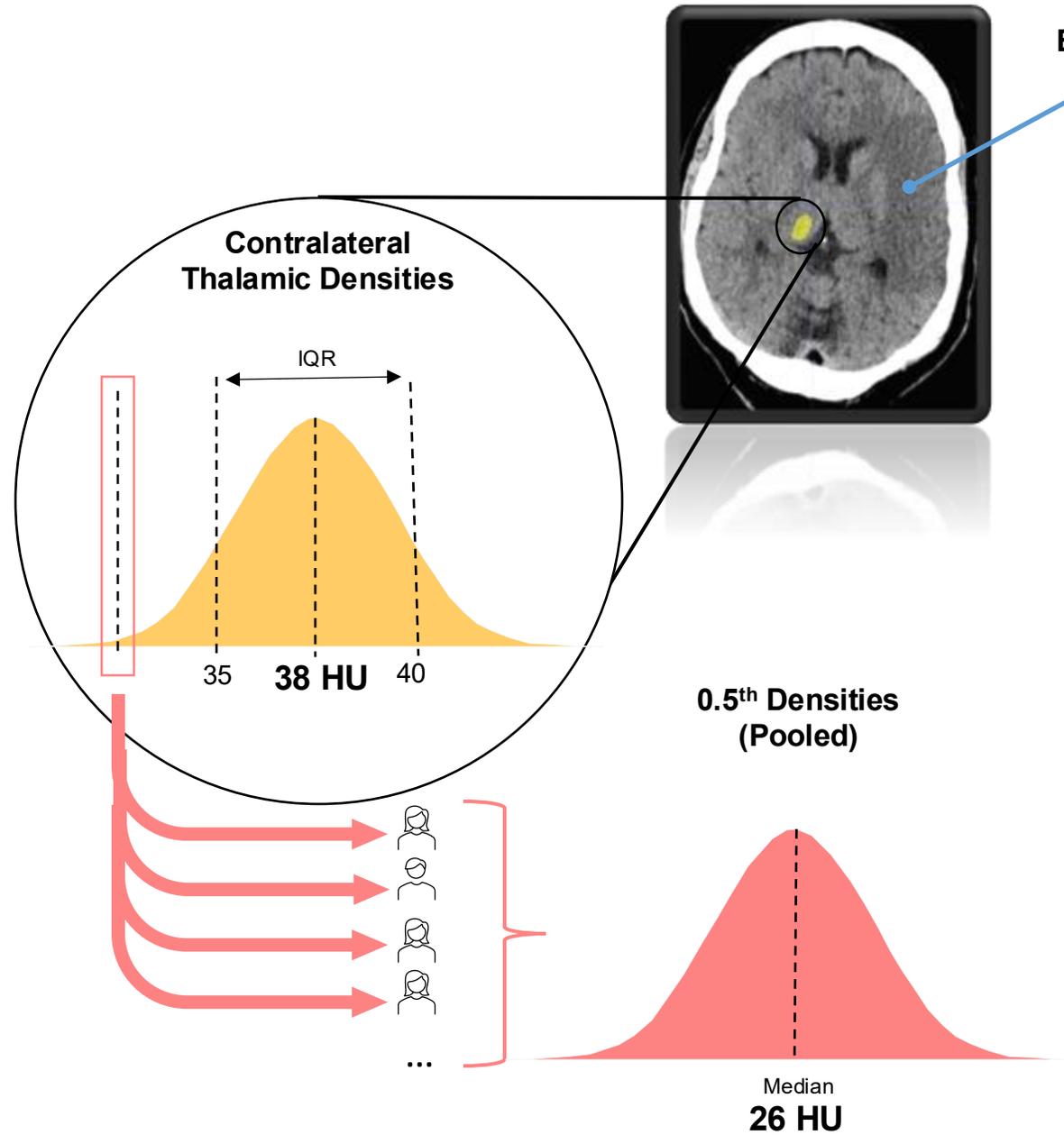
No Mismatch (1.8/15); aGenOR: 1.67, 95% CI: 1.23 to 2.27, p=0.001



ASPECTS

- Cortex vs subcortex
- Gray-white differentiation
- Window level settings
- Role of edema
- Shades of Grey





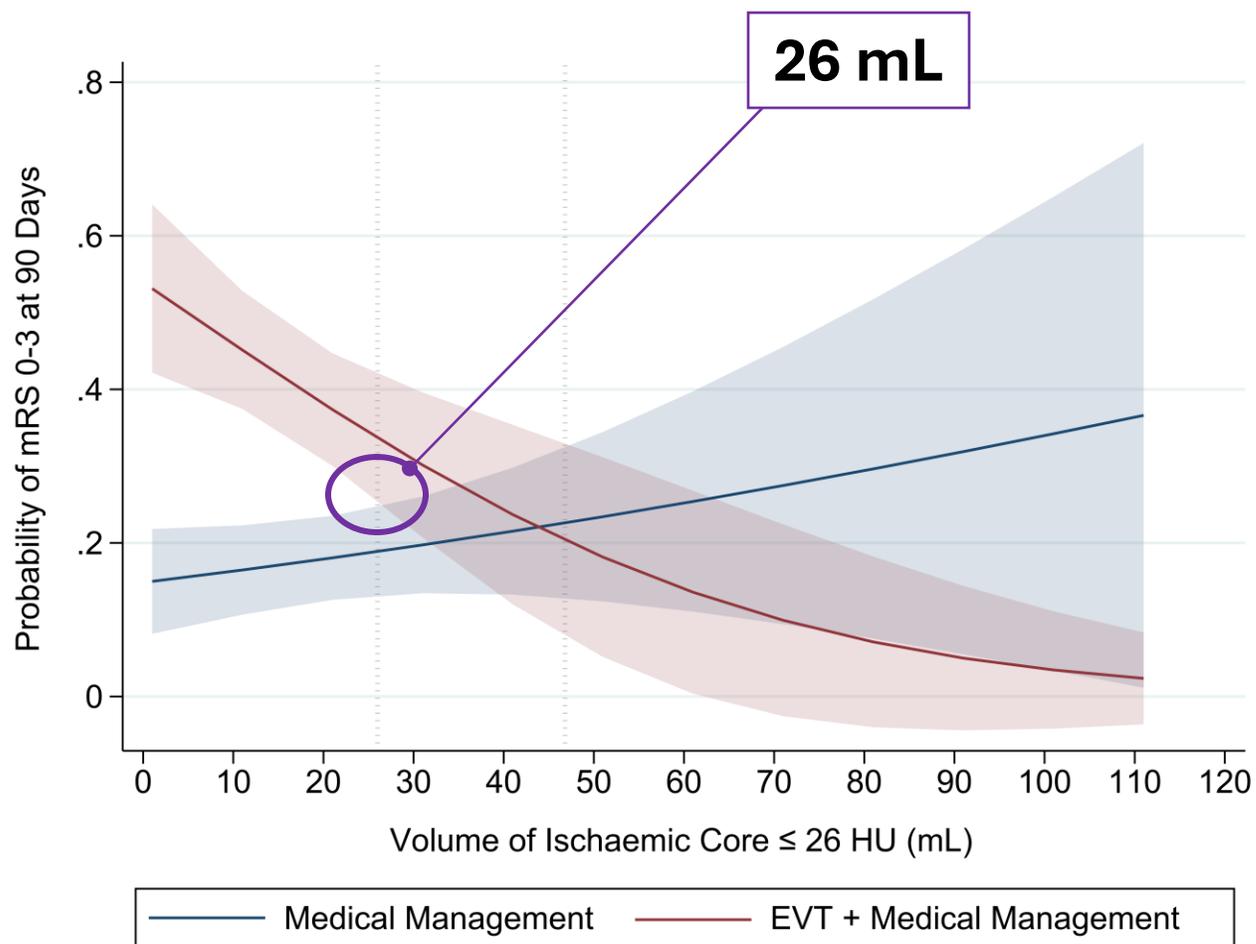
1

Defining Severe Hypodensity

- Median density of contralateral thalami:
 - 38 HU (IQR: 35-40)
- Median 0.5th Percentile CI
 - 26 HU (IQR: 23-29)

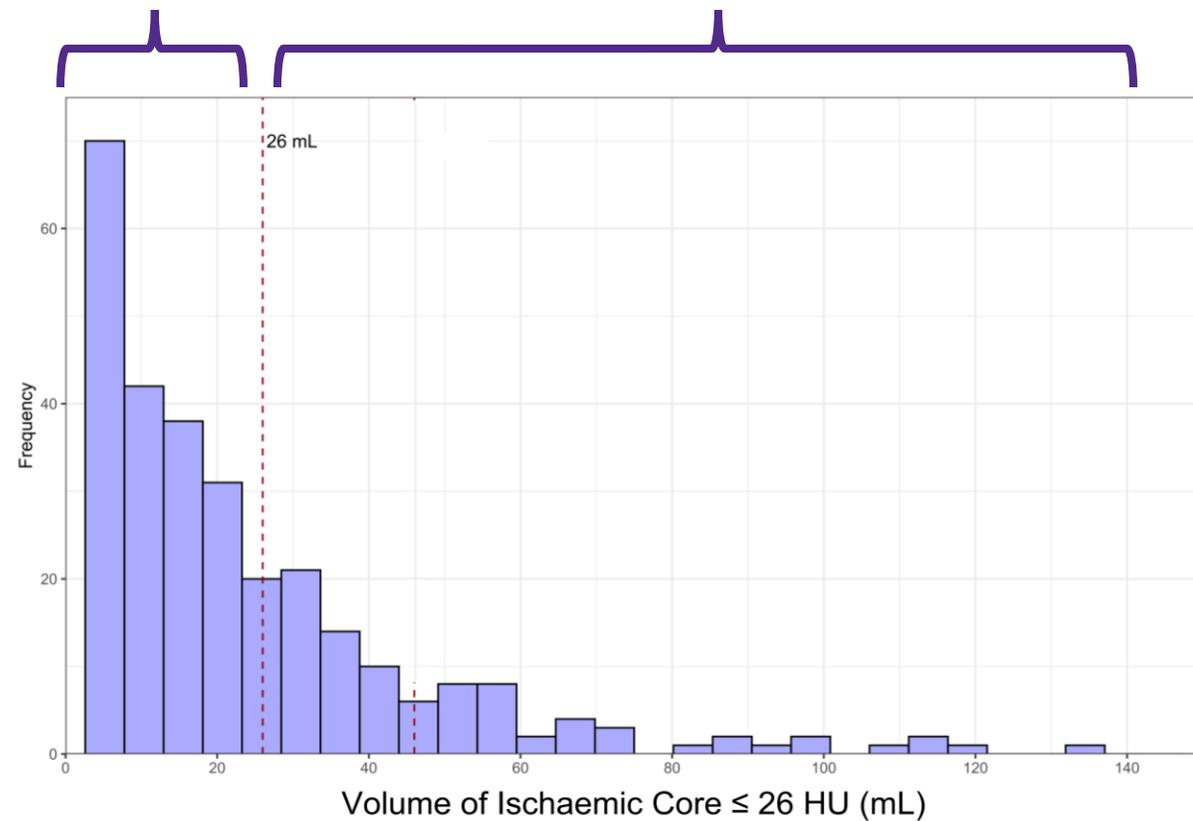
***Severe Hypodensity Threshold Selected:
26 HU***

Identifying a Clinically Relevant Volume



N=221

N=101



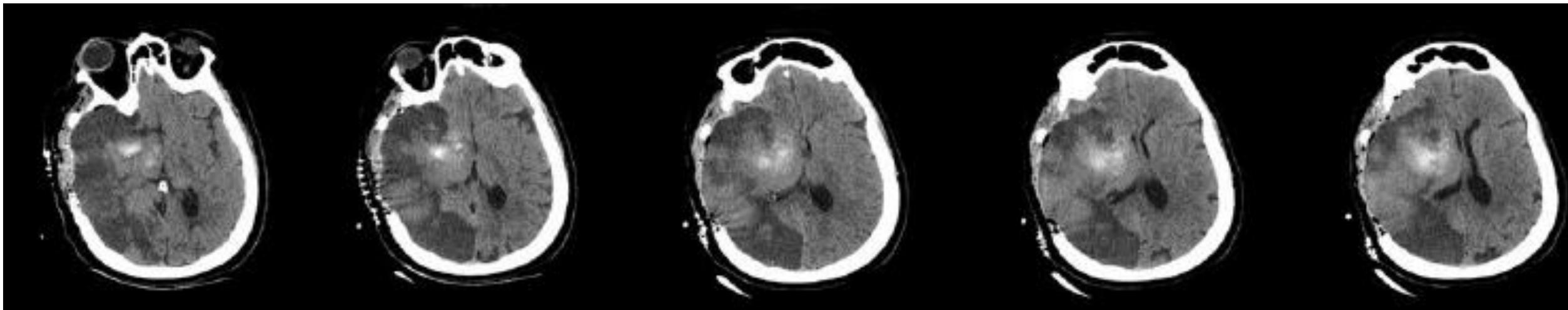
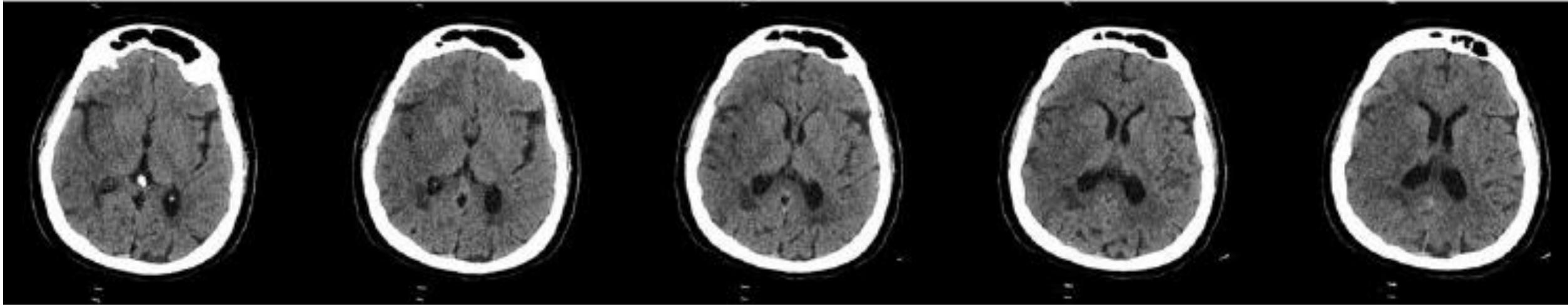
No significant benefit of EVT (vs MM) in patients with increasing volume of severe hypodensity on CT

Substantial volumes of severe hypodensity associated with more cerebral edema and higher need for hemicraniectomy after EVT



Association of Ischemic Core Hypodensity With Thrombectomy Treatment Effect in Large Core Stroke: A Secondary Analysis of the SELECT2 Randomized Controlled Trial

Yogendrakumar V et al. Stroke 2025

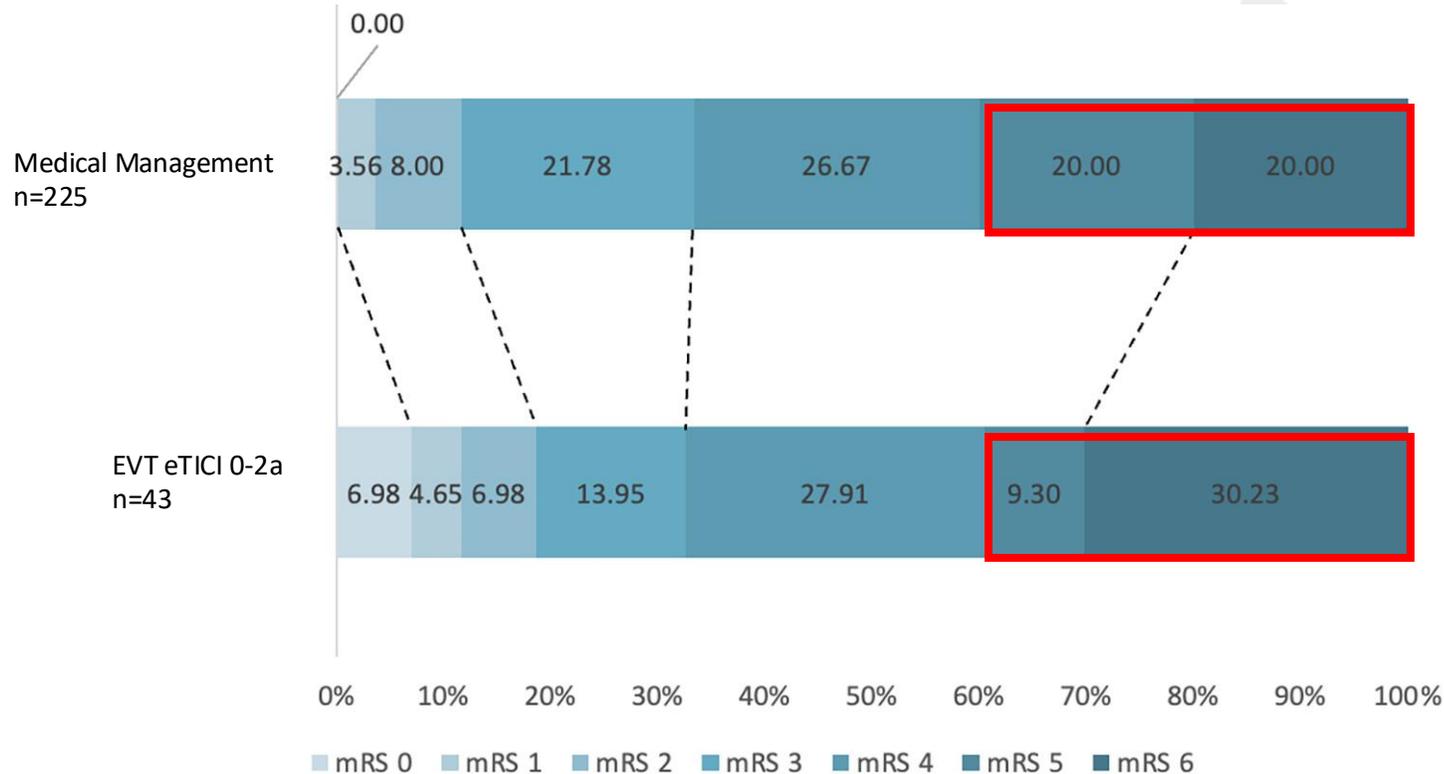




Unsuccessful Recanalization vs. Medical Management of Patients with Large Ischemic Core

Analysis of the ANGEL-ASPECT Randomized Trial

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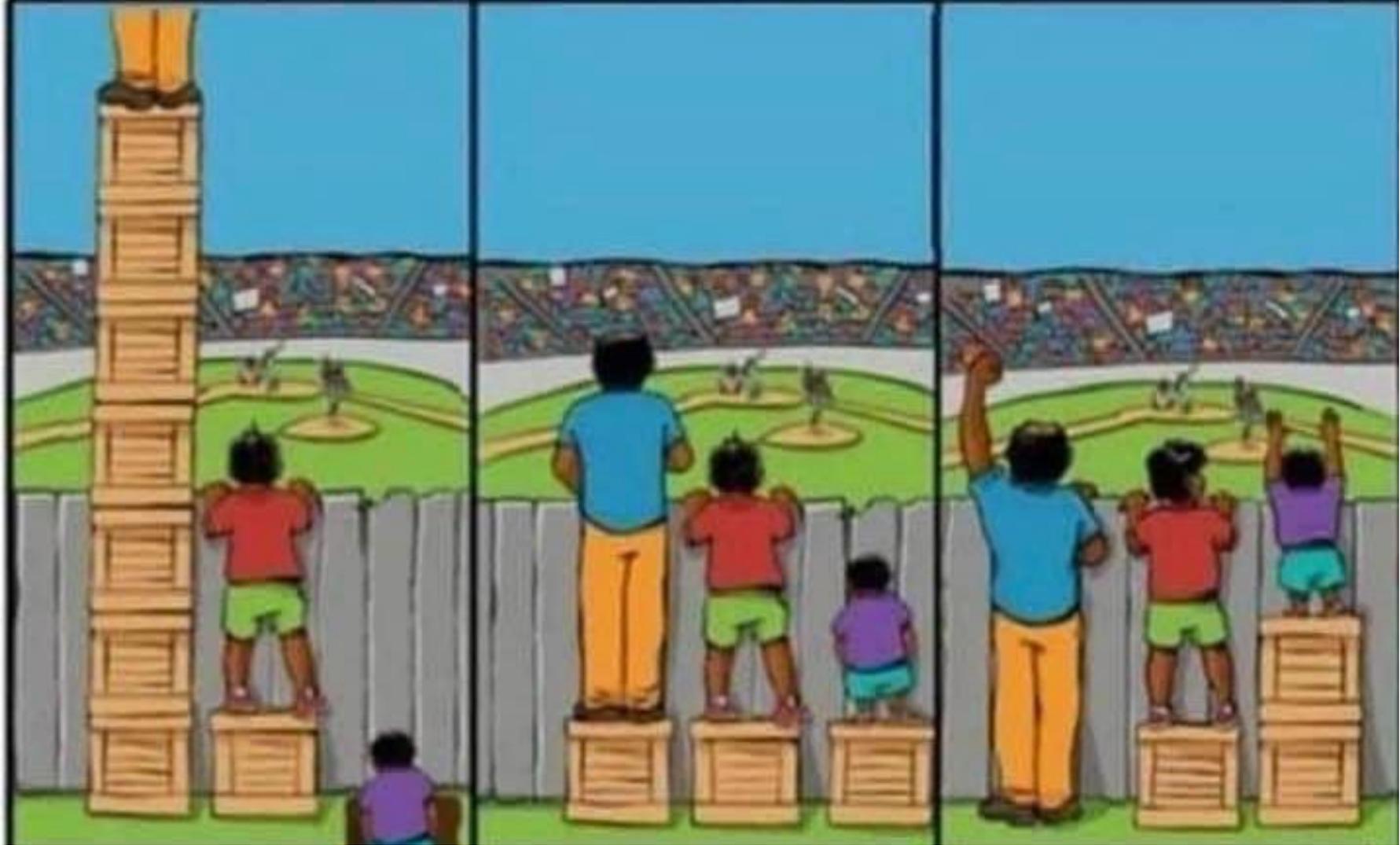


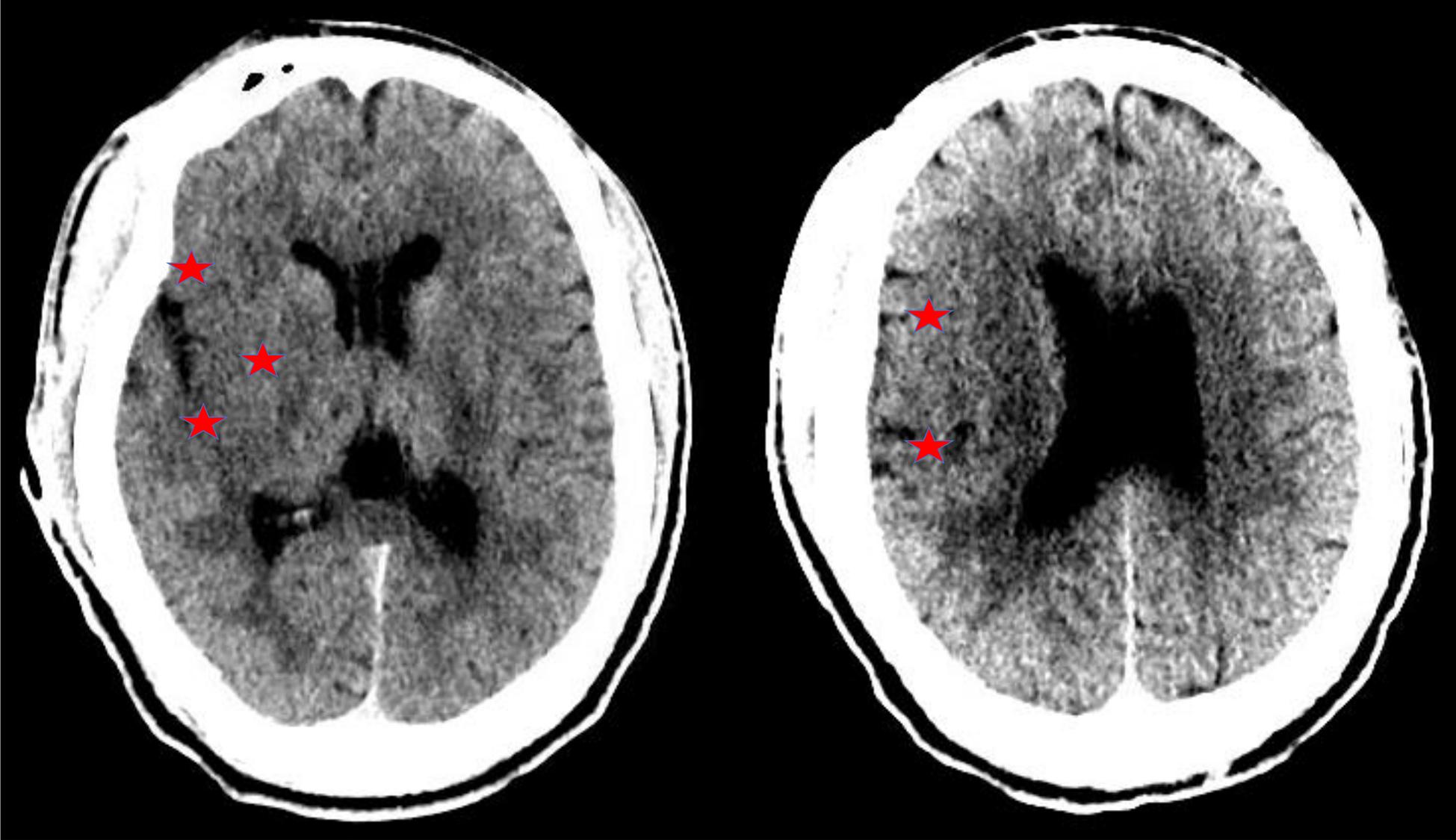
Unsuccessful EVT (vs. MM)

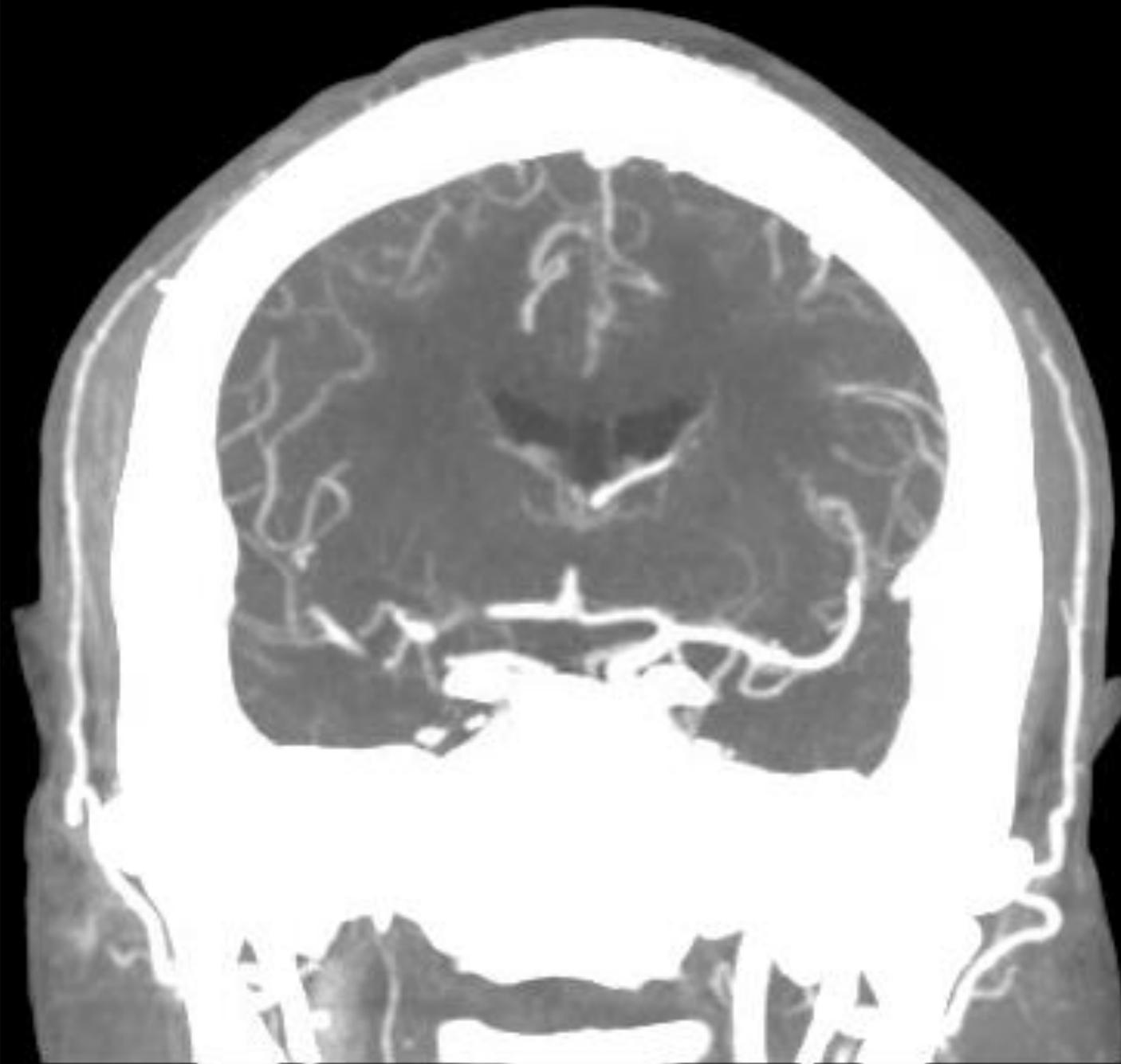
Higher ICH (55.8% vs. 17.3%, $p < 0.001$)

Infarct volume growth (142.7ml vs. 90.5ml, $p < 0.001$)

Craniectomy (18.6% vs. 3.6%, $p < 0.001$)

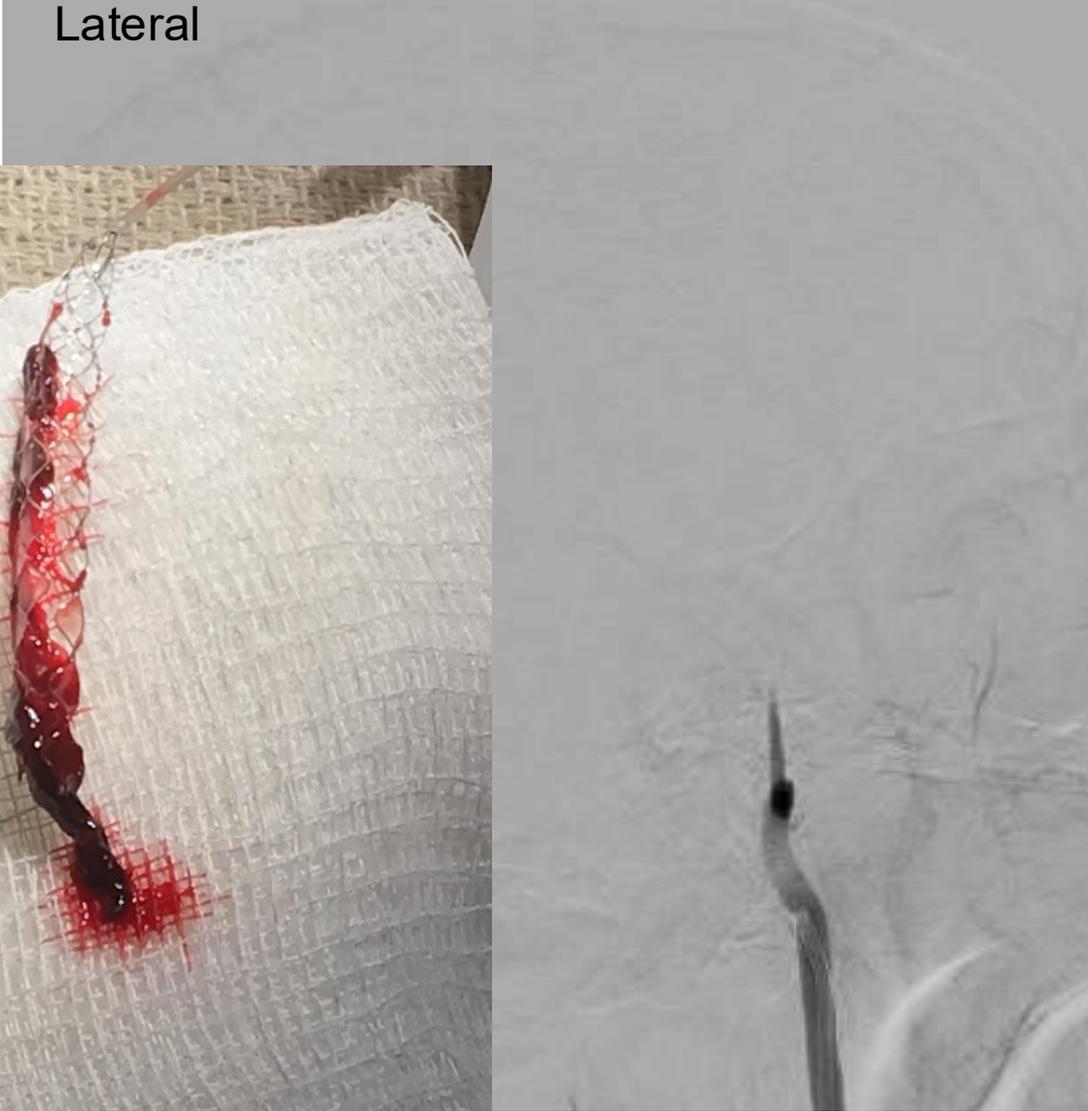
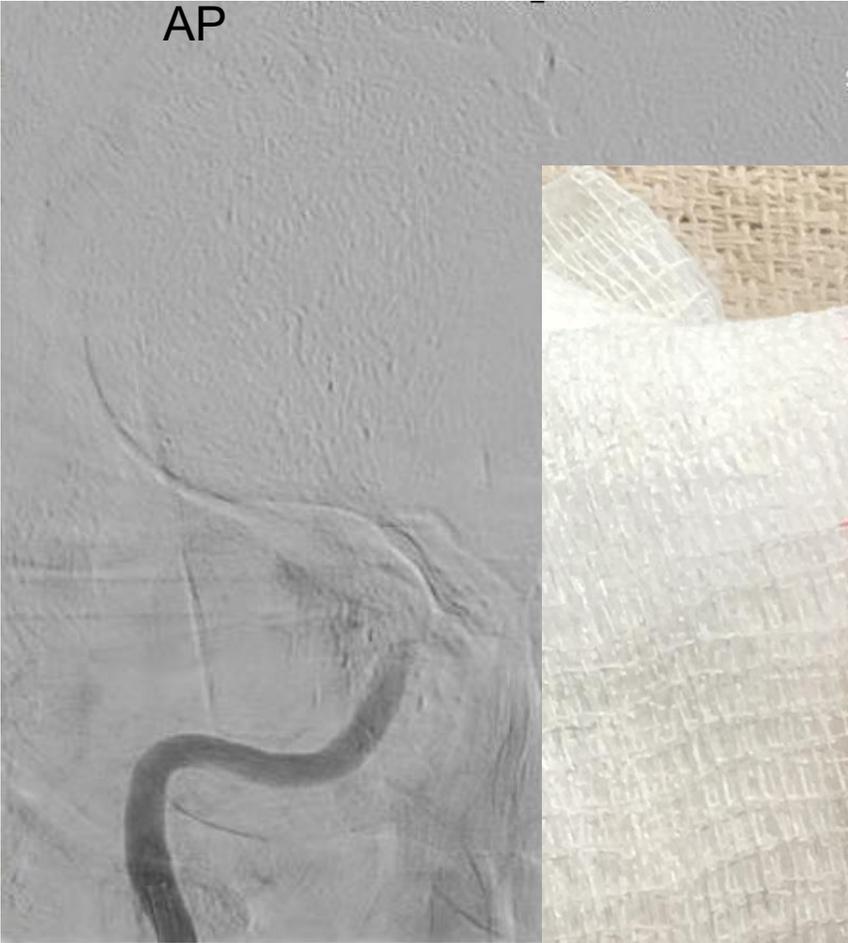




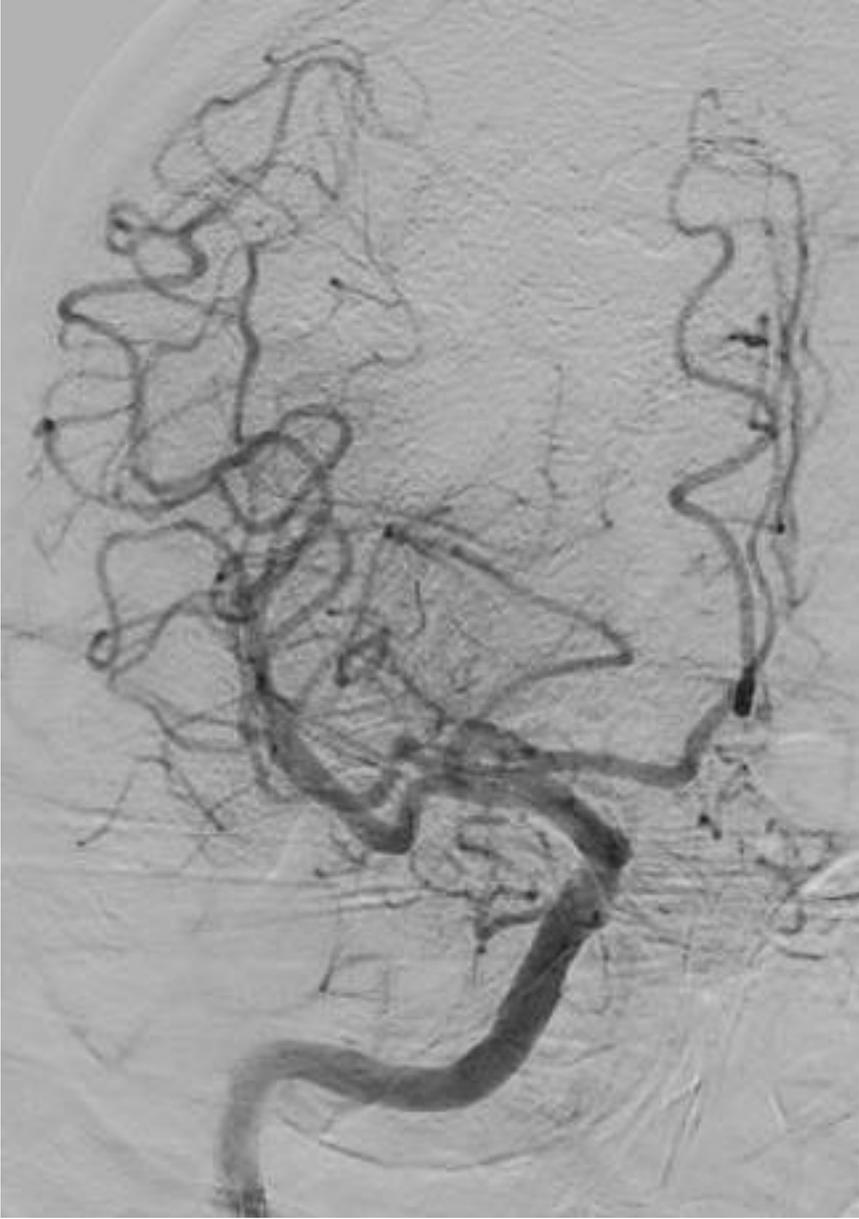


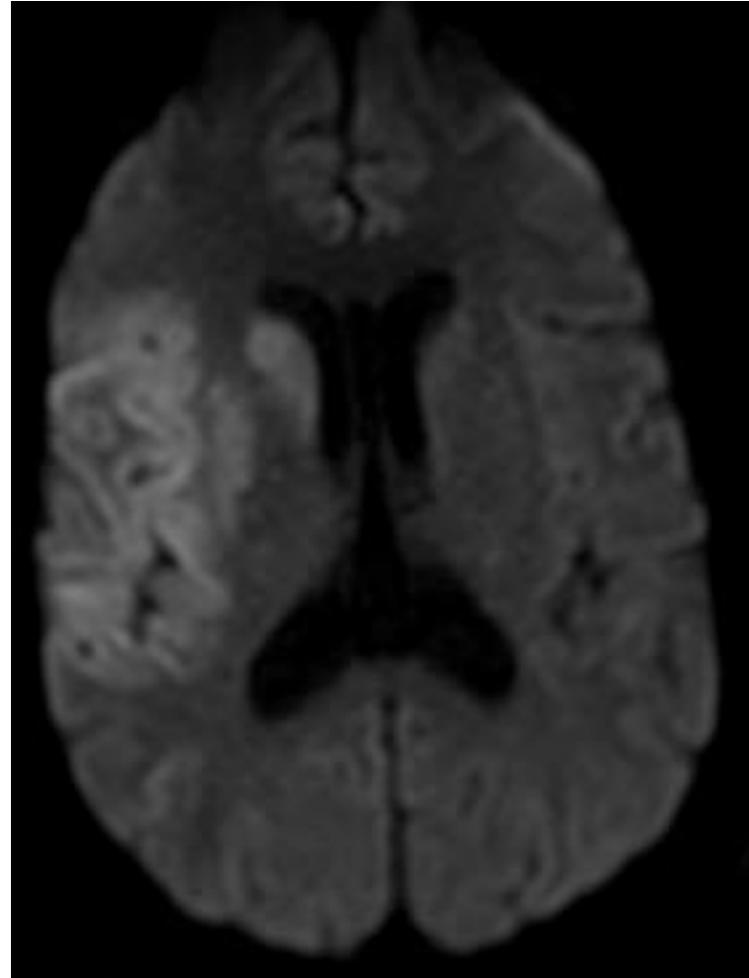
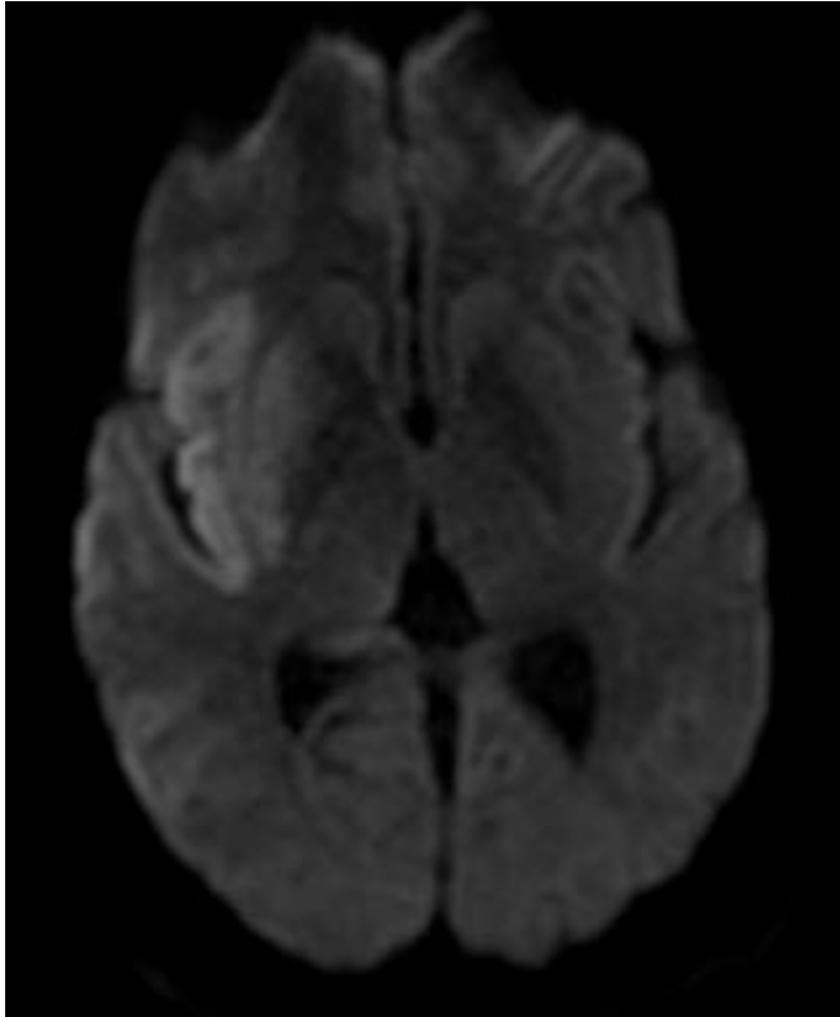
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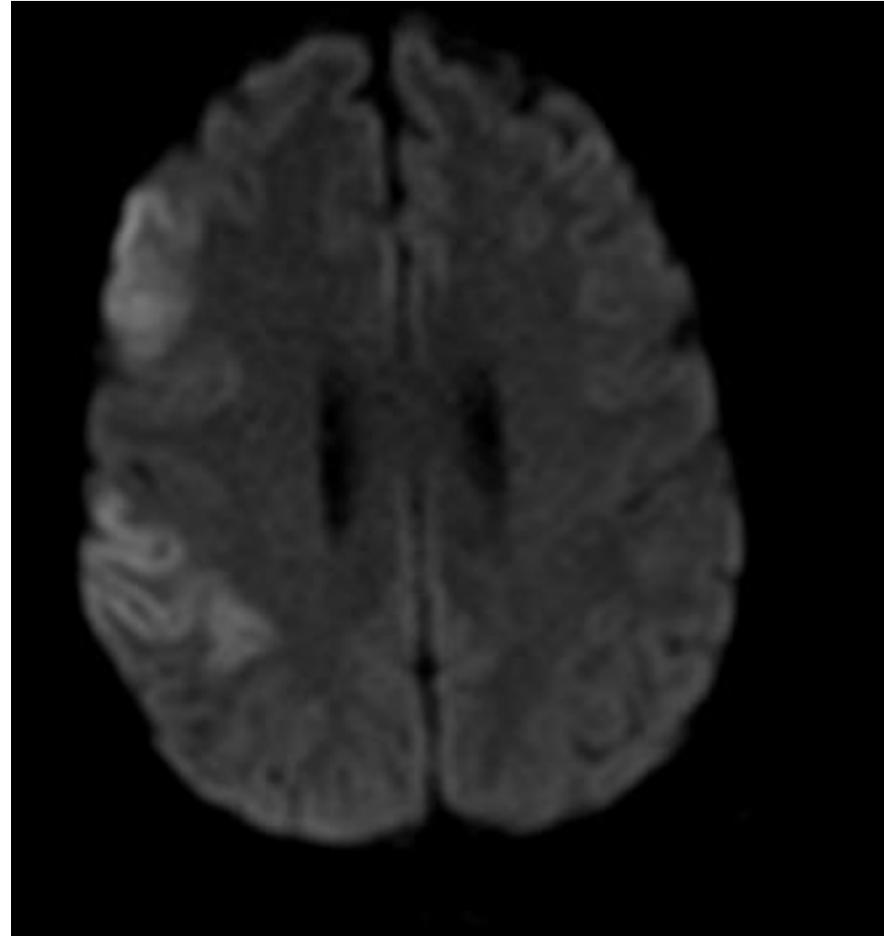
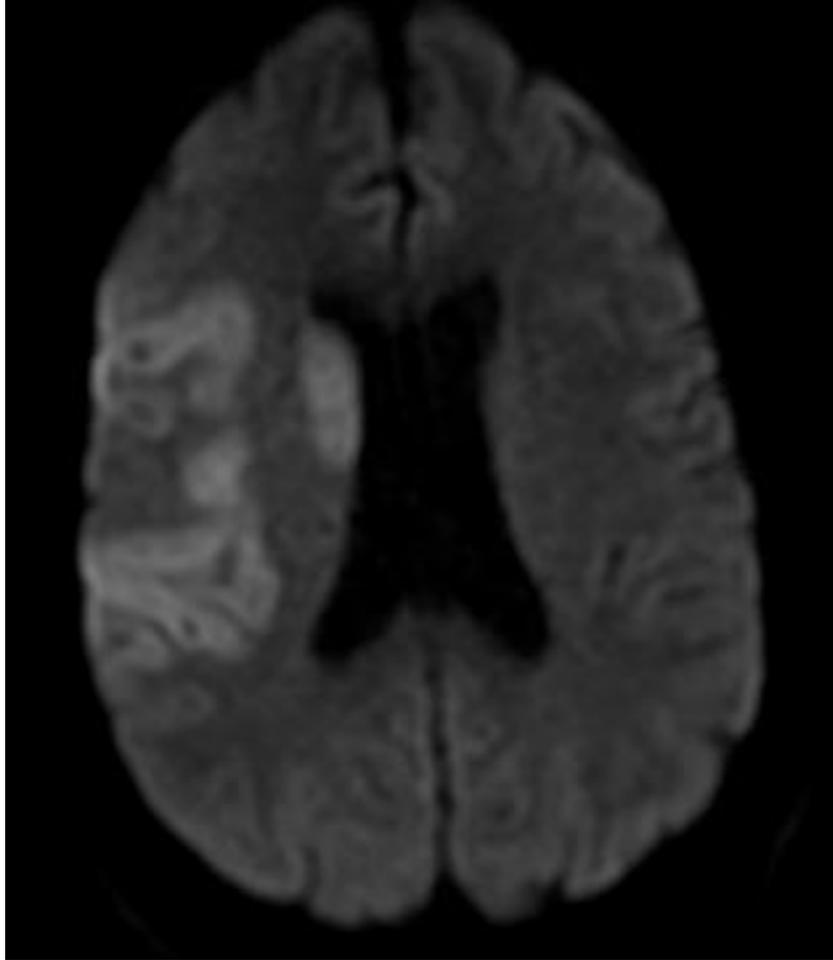
Lateral



NIHSS 18







Large Ischemic Core Gaps

- ASPECTS 0 to 2 with CT selection
- Degree of hypodensity
- Role of mismatch in small and large ischemic core stroke
- Adjunctive therapy

Conclusion

- Large ischemic core predicts lower likelihood of doing well with EVT but does not modify its treatment effect
- Earlier treatment with greater likelihood of benefit than later treatment
- ASPECTS 0 to 2 by NCCT uncertainty
- Even if there is no perfusion mismatch, EVT benefit seen
- The greater the volume of severity of hypodensity on CT scan, the lower the likelihood of EVT benefit vs. MM
- A simplified imaging protocol (CT/CTA) can be feasible for thrombectomy selection in light of large core data
(TESLA 1-year, TENSION, SELECT2, ANGEL-ASPECT)

