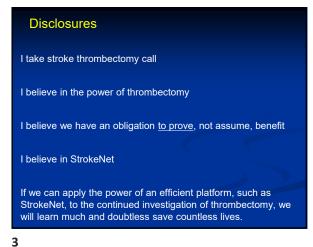
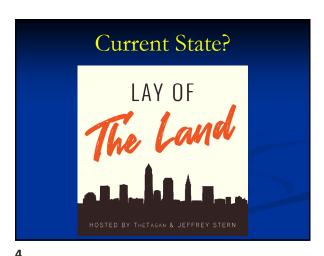
### Frontiers in Stroke Thrombectomy: MeVo, Large Core, Low NIHSS, Etc.

Disclosures National/International PI/Co-PI: INVEST (PI) COMPASS (Co-PI) THERAPY (PI) FEAT (PI) POSITIVE (Co-PI) PHIL (Co-PI) Investor: Cerebrotech, Imperative Care, Endostream, Viseon, BlinkTBI, Serenity, Cardinal Consulting, NTI, RIST, Viz.ai, Synchron, Truvic nsultant: Imperative Care, Cerebrotech, Viseon, Endostream, Vastrax, RIST, Synchron, Viz.ai, rflow, Viz.ai, CVAid

1 2





### **Current State:** AHA/ASA Guideline Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association Endorsed by the Society for Academic Emergency Medicine and The Neurocritical Care Society Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons.

**Current State:** Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age  $\geq$ 18 years; (4) NIHSS score of  $\geq$ 6; (5) ASPECTS of  $\geq$ 6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.

6

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Direct aspiration thrombectomy as first-pass mechanical thrombectomy is recommended as noninferior to stent retriever for patients who meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or M1; (3) age  $\geq$ 18 years; (4) NIHSS score of  $\geq$ 6; (5) ASPECTS  $\geq$ 6; and (6) treatment initiation (groin puncture) within 6 hours of symptom onset.

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### Patients with Pre-Stroke Disability

Patients should receive mechanical thrombectemy if they meet all the following criteria (1) prestroke mRS score of 0 to 1;2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.

Patients with Pre-Stroke Disability

### Mechanical Thrombectomy in Patients With Ischemic Stroke With Prestroke Disability

Sanjana Salwi, BA\*; Shawna Cutting, MD\*; Alan D. Salgado, MD; Kiersten Espaillat, DNP; Matthew R. Fusco, MD; Michael T. Froehler, MD, PhD; Rohan V. Chitale, MD; Howard Kirshner, MD; Matthew Schrag, MD, PhD; Adam Jasne, MD; Tina Burton, MD; Brian MacGrory, MB BCh, BAO, MRCP; Ali Saad, MD; Mahesh V. Jayaraman, MD; Tracy E. Madsen, MD, ScM; Katarina Dakay, DO; Ryan McTaggart, MD; Shadi Yaghi, MD; Pooja Khatri, MD, MS; Akshikkumar M. Mistry, MD; Eva A. Mistry, MBBS

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### Patients with Pre-Stroke Disability

Prospective observational study across 2 CSCs

761 mRS 0-3 patients 2 cohorts; mRS 0-1 v. mRS 2-3

Good outcome:

90-d mRS 0-1 or no worsening of prestroke mRS

Patients with Pre-Stroke Disability

mRS 0-1: 36.7% versus 26.7%, p=0.008

### Patients with Pre-Stroke Disability

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Multivariate Analysis: OR 0.90 [0.60–1.35], P=0.6 Propensity Score Matched: OR 1.16 [0.75–1.8], P=0.49

13

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Higher Mortality in disabled patients 14% vs 40%, P<0.001

34% of ant. circulation thrombectomy patients mRS 2-3

15

### MeVo and other distal occlusions

Patients should receive mechanical thrombectomy
they meet all the following eriteria: (1) prestroke mRS score of 0 to 1; (2)
Causative occlusion of the internal carotid artery or MCA segment 1 (M1); 
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Higher Mortality in disabled patients 14% vs 40%, P<0.001

14

### Patients with Pre-Stroke Disability

Although its benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for patients with AlS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score >1, ASPECTS <6, or NIHSS score <6, and causative occlusion of the internal carotid artery (ICA) or proximal MCA (M1).

We need RCTs

16

### MeVo and other distal occlusions

<u>Stroke</u>

SPECIAL REPORT

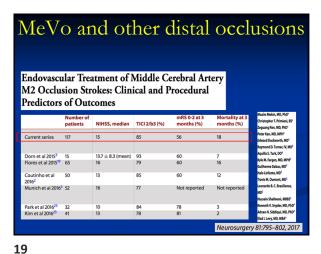
Thrombectomy for Distal, Medium Vessel Occlusions

A Consensus Statement on Present Knowledge and Promising Directions

Jeffrey L. Saver, MD; Rene Chapot, MD; Ronit Agid, MD; Ameer E. Hassan, DO; Ashutosh P. Jadhav, MD; David S. Liebeskind, MD Kyriakos Lobotesis, MD; Dan Melle MD; Lukas Meyer, MD; Guy Raphaell, MD; Rishi Gupta, MD; for the Distal Thrombectomy Summit Group\*1

Distal Occlusions 24-40% of AIS

IV tPA fails to recanalize 1/3 to 1/2 of such occlusions



MeVo and other distal occlusions Endovascular Treatment of Middle Cerebral Artery M2 Occlusion Strokes: Clinical and Procedural Predictors of Outcomes NIHSS, media TICI 2/b3 (%) Current series 117 Park et al 2016<sup>23</sup> 32 Kim et al 2016<sup>25</sup> 41

20

MeVo and other distal occlusions Efficacy of endovascular thrombectomy in patients with M2 segment middle cerebral artery occlusions: metaanalysis of data from the HERMES Collaboration Bijoy K Menon,<sup>1</sup> Michael D Hill,<sup>2</sup> Antoni Davalos,<sup>3</sup> Yvo B W E M Roos,<sup>4</sup> Bruce C V Campbell,<sup>5,6</sup> Diederik W J Dippel,<sup>7</sup> Francis Guillemin,<sup>8,9</sup> Jeffrey L Saver,<sup>10</sup> Aad van der Lugt,<sup>11</sup> Andrew M Demchuk,<sup>12</sup> Keith Muir,<sup>13</sup> Scott Brown,<sup>14</sup> Tudor Jovin,<sup>15</sup> Peter Mitchell,<sup>16</sup> Phil White,<sup>17,18</sup> Serge Bracard,<sup>19</sup> Mayank Goyal<sup>20</sup> Menon BK, et al. J NeuroIntervent Surg 2019;11:1065-1069. doi:10.1136/neurintsurg-2018-014678

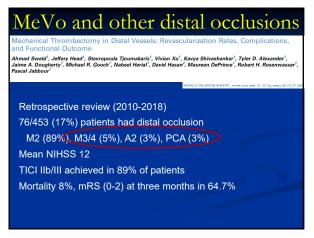
MeVo and other distal occlusions 12 EVT Control Control group, % (n/N) Odds ratio (95% CI) Odds ratio (95% CI) 58.2% (39/67) 39.7% (25/63) 2.13 (1.05 to 4.35) 0.04 2.39 (1.08 to 5.28) 0.03 Menon BK, et al. J NeuroIntervent Surg 2019;11:1065-1069. doi:10.1136/neurintsurg-2018-01467

22

21

MeVo and other distal occlusions 1.91 (0.72 to 5.1) 4.08 (1.08 to 15.48) Menon BK, et al. J NeuroIntervent Surg 2019;11:1065-1069. doi:10.1136/neurintsurg-2018-014678

Retrospective review (2010-2018) 76/453 (17%) patients had distal occlusion M2 (89%), M3/4 (5%), A2 (3%), PCA (3%) Mean NIHSS 12 TICI IIb/III achieved in 89% of patients Mortality 8%, mRS (0-2) at three months in 64.7%



MeVo and other distal occlusions

Mechanical Thrombectomy in Distal Vessels: Revascularization Rates, Complications, and Functional Outcome

Ahmad Sweid', Jeffery Head', Stavropoula Tjournakaris', Vivian Xu', Kavya Shivashankar', Tyler D. Alexander', Jaine A. Dougherry', Michael R. Gooch', Nabeel Herial', David Hasan', Maureen DePrince', Robert H. Rosenwasser', Pascal Jabbour'

Retrospective review (2010-2018)

76/453 (17%) patients had distal occlusion

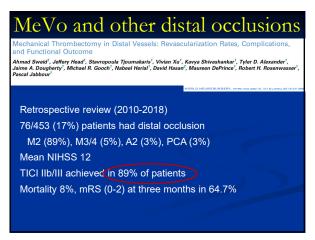
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25 26



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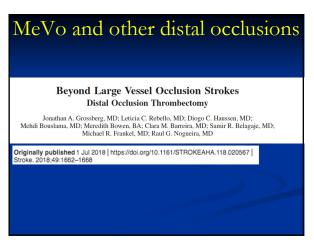
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Mean NIHSS 12

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27 28



MeVo and other distal occlusions

Retrospective review

69 patients with distal thrombectomies
out of 949 patients in database

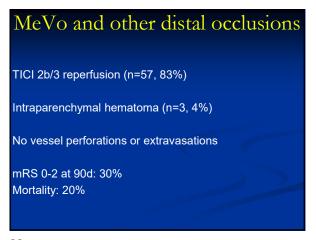
ACA, PCA, MCA opercular (M3) and beyond

# MeVo and other distal occlusions 42% received intravenous tPA Median NIHSS 18 Distal occlusion primary location in 45 patients 23 patients - distal occlusion thrombectomy was a rescue strategy after successful proximal LVO

MeVo and other distal occlusions

Location (primary distal)→45 patients
 MCA-M3 (n=21)
 ACA alone (n=8)
 ACA with concomitant MCA-M1/MCA-M2 (n=10)
 ACA with concomitant MCA-M3 (n=3)
 PCA (n=3)
Location (rescue)→23 patients
 MCA-M3 (n=11)
 ACA (n=7)
 PCA (n=4)
 MCA-M3 and ACA (n=1)
One patient had both primary and rescue
 ACA (primary) and MCA-M2 (proximal LVO) occlusions treated, followed by rescue MCA-M3 (distal) thrombectomy

31 32



MeVo and other distal occlusions

83 yo F with HTN, Afib and CHF presented with acute onset aphasia, L gaze deviation and R side weakness

NIHSS 17

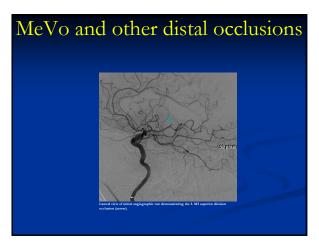
Head CT ASPECTS 10

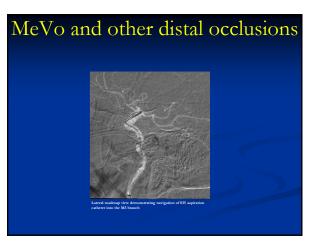
CTA suggesting distal L MCA M3/M4 occlusion

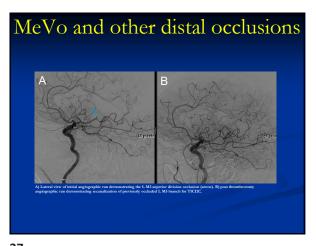
Patient out of window for IV thrombolytic therapy

34

33

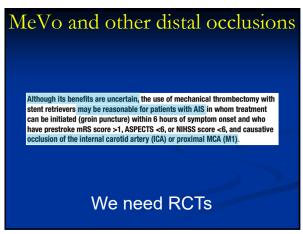






## MeVo and other distal occlusions Patient significant improved complete resolution of hemiplegia moderate residual expressive aphasia NIHSS 3

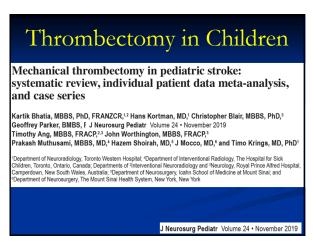
37 38



Patients should receive mechanical thrombectomy
if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2)
causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3)
age ≥18 years: (A) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment
can be initiated (groin puncture) within 6 hours of symptom onset.

40

39



Thrombectomy in Children

We need Registries

# Patients should receive mechanical thrombectomy they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.

### **Epidemiology of minor Stroke**

790K annual incidence of stroke in the US. 87% ischemic.

35-50% of acute ischemic stroke are minor stroke symptoms (MSS).

Mozeffarian D, Berjamin EJ, Go AS, Arnett DK, Bisha MJ, Cushman M, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. Oriculation: 2015 Januari 14(1):e23–22 The W, Churilov L, Campbell BCV, Lin M, Liu X, Davis SM, et al. Does Large Vessel Octuation Affect offinical Outcome in Stroke with Mild Neurological Control of Stroke and Cerebrovascular Diseases. 2014 Nov.23(1):2383–5. Nov. 14(1):e33–6. Nov. 14(1):e345–6. Nov

43 44

### Natural history of minor stroke

23.5% of MSS with unfavorable outcome.

Early neurological deterioration is common.

Nedeltichev K, Schwegler B, Hasfell T, Brekerfeld C, Gralla J, Fischer U, et al. Outcome of Stroke With Mild or Rapidly Improving Symptoms. Stroke. 2007 Jul 27:1489;2531-4 Kim JT, Heb S-H, Yoon W, Chol K-H, Park M-S, Saver JL, et al. Clinical outcomes of patients with acute minor stroke receiving rescue IA therapy follows: Early Neurological Deterioration

Early neurological deterioration (END): 23-41%

Associated with worse outcome - up to 60% poor outcome

LVO increases the risk of END (OR 2.2) and is present in 44% of patients with END.

Occurs within 5-16 h of presentation.

Kim J.T., Ho S.H. Yoon W, Cho K.H. Park M.S., Saver JL, et al. Clinical customes of patients with acute minor stroke receiving rescue IA therapy following early neurological deterioration. Journal of NeuroInterventional Surgery, 2015 Apr 15, 18(5), 6415-18.

Kim J.T., Park M.S., Chang J., Lee J.C., Dark F.Y., Cho K.H. Proximal Affaila Occidation in Anche schamic Stroke with Low NIMSS Scores Should Not Be Considered as Mild Stroke Survey.

46

45

### Epidemiology of LVO in Minor stroke

Up to 70% of patients with MSS, do not undergo vessel imaging.

Annual incidence of MSS-LVO is ~70K per year.

Kim J-T, Heo S-H, Yoon W, Choi K-H, Park M-S, Saver JL, et al. Clinical outcomes of patients with acute minor stroke receiving rescue IA therapy following early

### Natural History of MSS-LVO

MSS-LVO - 7.13 odds of poor outcome (CI 1.1–45.5, p < 0.038)

Untreated MSS-LVO - 32-45% poor outcome.

6% mortality

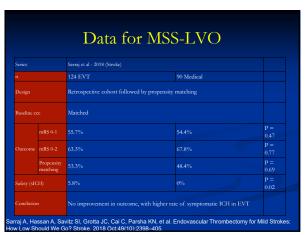
Heldner MR, Jung S, Zubler C, Mordasini P, Weck A, Mono ML, et al. Outcome of patients with occlusions of the internal carotid artery or the main stem of the middle cerebral artery with NiHSS score of less than 5: comparison between thrombolysed and non-thrombolysed patients. Journal of Neurology, Neurosurgery & Psychiatry, 2013, Jun 1236(7):755-60.



49 50

	D	ata for M	SS-LVO	
Series n Design		Bowen et al, 2017	Dargazanli et al, 2017	Pfaff et al, 2016 33 Retrospective, single arm
		72 Retrospective, single center, single arm	Retrospective, single arm, Matched control analysis	
Other				
Favorable Outcome	72%	78.3%	63.6%	
Complication		6% ICH, 10% 90 day mortality	5.1% mortality	15.1% occult SAH 6.1% mortality
		Successful reperfussion independent predictor of good outcome	Successful recanalization associated with better outcome OR 3.09 (CI 1.06- 9.03).	

51 52



Data for MSS-LVO

Proximal (ICAT + M1) occlusions
Dichotomized outcome: 53% EVT vs 30% Medical Management
OR 2.68; 95% CI 0.98-7-32

Distal (M2-M4 + ACA) occlusions

No Difference

Sarraj A, Hassan A, Savitz SI, Grotta JC, Cal C, Parsha KN, et al. Endovascular Thrombectomy for Mild Strokes: How Low Should We Go? Stroke, 2018 Oct,49(10):238-465.

			or MSS-L	
		Messer et al - 2017 (AJNR)		
		8 immediate EVT	6 delayed EVT	40 Medical
		Retrospective		
Baseline ccc		Prospectively collected concurrent medical treatment		
		75%	33%	55%
Safety (sICH)		0%	0%	0%
		Promising signal		

Low NIHSS

JAMA Neurology | Original Investigation

Medical Management vs Mechanical Thrombectomy for Mild Strokes

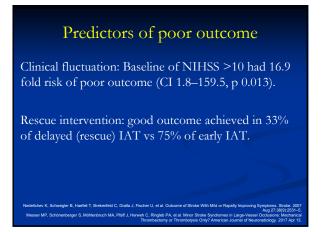
An International Multicenter Study and Systematic Review
and Meta-analysis

Nisin Goyal, MD, Georgio Tsingoulis, MD, Konark Malbora, MD, Muhammad F, Ishfaq, MD, Abhi Pandis, MD, Michael T, Frobler, MD,
Algandro N, Sportz, MD, Bidummad Anadis, MD, Marios Psychologo, MD, Voller Mana, MD, Admin Sidoga, MD, Mahmmad Yanga, MD,
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Rome Laker, MD, Jose E, Cohen, MD, Arindelei H, Kistanos, MD, Georgoo Magodin, MD, Blackobo Psychogo, MD, Vollerio Loutas, MD,
Rome Laker, MD, Jose E, Cohen, MD, Arindelei H, Kistanos, MD, Georgoo Magodin, MD, Roderobo Psychogo, MD, Volleios Loutas, MD,
Rev Pankolstand, MD, Vigilica Inoa, MD, Daniel Holt, MD, MPH; Lucas Eljovich, MD, Andrei V, Alexandrov, MD, Admin S, Arthur, MD, MPH

251 patients (138 ST v. 113 MM)

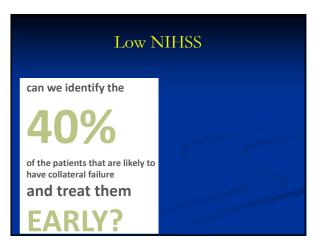
No benefit in outcome

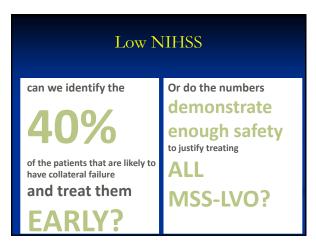
55 56

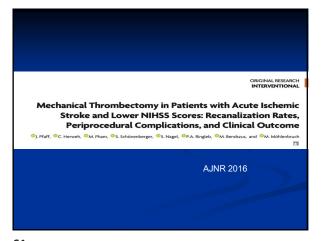


END is associated with poor outcome
IAT protects against END
Early IAT is better than rescue IAT
But IAT is not without risks (up to 12% sICH)
Better way of identifying and selecting patients at risk of END

57 58







33 pts NIHSS < 8

Median post procedure NIHSS 5

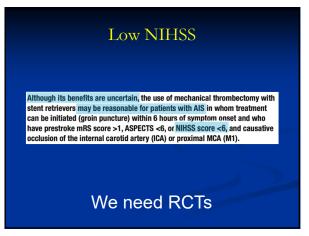
Recanalization of TICl 2b or 3
achieved in 79%

6% symptomatic ICH

mRS 0-2 633%

mRS 0-3 in 91%

61 62



Patients should receive mechanical thrombectomy
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63 64

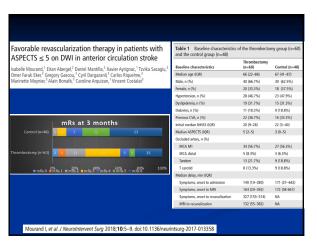
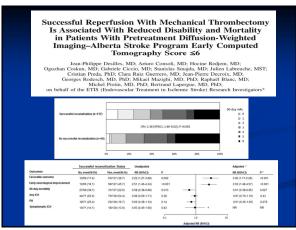


Table 2 Outcomes of the thrombectomy group (n=60) and the control group (n=48) Thrombectomy Outcomes (n=60)Control (n=48) Successful recanalization, n (%) 45 (75%) NA Clinical outcome at 90 days, n (%) mRS ≤2 18 (30%) 1 (2.1%) sICH 3 (6.3%) 3 (5%) Malignant Infarction 5 (8.3%) 9 (18.8%) Hemicraniectomy 2 (3.3%) 11 (22.9%) 15 (25%) 23 (47.9%) Mortality Mourand I, et al. J NeuroIntervent Surg 2018;10:5–9. doi:10.1136/neurintsurg-2017-013358



67 68

JAMA Neurology | Original Investigation

Outcomes of Endovascular Thrombectomy vs Medical Management Alone in Patients With Large Ischemic Cores A Secondary Analysis of the Optimizing Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke (SELECT) Study

Amrou Sarraj, MD. Ameer E. Hassan, DO, Sean Savitz, MD, Clark Sitton, MD. James Grotta, MD, Peng Chen, MD, Chunyan Cai, PhD, Gay Cutter, PhD, Bita Imam, PhD, Sajan RedQ, MD, Kauchik Parsha, MD, Deep Pajara, MD, Roy Riascos, MD, Rinze viora, MD, Michael Abraham, MD, Haris Kamal, MD, Clago C. Hausen, MD, Andrew D, Barreto, MD, Maarten Landere, MD, Rich Gildur, MD, Gregory W, Albers, MD

105 patients with large core

mRS 0-2: 31% EVT v 14% MM or 3.27 [1.11-9.92], p=0.03

69

### Large Core

Triage imaging and outcome measures for large core stroke thrombectomy – a systematic review and meta-analysis

Amrou Sarraj,  $^1$  James C Grotta,  $^2$  Deep Kiritbhai Pujara,  $^1$  Faris Shaker  $^{\odot}$  ,  $^1$  Georgios Tsivgoulis  $^{3,4}$ 

Pooled Random Effect Meta-analysis of 12 studies mRS 0-2: 25% v 7% OR 4.39 [2.53, 7.64], p<0.00001 Mortality: 23% v 33% OR 0.53 [0.40, 0.71], p<0.0001 sICH: 9% v 5% OR 1.68 [0.92, 3.09], p<0.09

Sarraj A, et al. J NeuroIntervent Surg 2020;12:1172–1179. doi:10.1136/neurintsurg-2019-015509

Acute Stroke With Large Ischemic Core Treated by Thrombectomy

**Predictors of Good Outcome and Mortality** 

Pietro Panni, MD; Benjamin Gory, MD, PhD; Yu Xie, MD, PhD; Arturo Consoli, MD; Jean-Philippe Desilles, MD, PhD; Mikael Mazighi, MD, PhD; Julien Labreuche, BST; Michel Piotin, MD, PhD; Francis Turjman, MD, PhD; Omer Faruk Eker, MD, PhD; Serge Bracard, MD; René Anxionnat, MD, PhD; Sébastien Richard, MD, PhD; Gabriela Hossu, PhD; Raphael Blanc, MD, MSc; Bertrand Lapergue, MD, PhD; on behalf of the ETIS (Endovascular Treatment in Ischemic Stroke) Investigators\*

Successful Recanalization strongly predicted outcome adj OR 4.56 [1.79–11.62]; P=0.001

JAMA Neurology | Original Investigation

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105 patients with large core

mRS 0-2: 31% EVT v 14% MM OR 3.27 [1.11-9.92], p=0.03

RCTs are needed

70

### Large Core

Triage imaging and outcome measures for large core stroke thrombectomy – a systematic review and meta-analysis

Amrou Sarraj, <sup>1</sup> James C Grotta, <sup>2</sup> Deep Kiritbhai Pujara, <sup>1</sup> Faris Shaker <sup>o</sup>, <sup>1</sup> Georgios Tsivgoulis<sup>3,4</sup>

Pooled Random Effect Meta-analysis of 12 studies mRS 0-2: 25% v 7% OR 4.39 [2.53, 7.64], p<0.00001 Mortality: 23% v 33% OR 0.53 [0.40, 0.71], p<0.0001 sICH: 9% v 5% OR 1.68 [0.92, 3.09], p<0.09

RCTs are needed

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