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Análisis mediante RM avanzada del estado de reperfusión cerebral tras fibrinólisis adyuvante a trombectomía mecánica

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Carlos Laredo Gregorio

Neurociencias clínicas y experimentales

Enfermedades cerebrovasculares

Nuestro grupo investiga estrategias que mejoren la calidad de vida de los pacientes al optimizar su riego sanguíneo cerebral

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JAMA | Preliminary Communication

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Effect of Intra-arterial Alteplase vs Placebo Following Successful Thrombectomy on Functional Outcomes in Patients With Large Vessel Occlusion Acute Ischemic Stroke

The CHOICE Randomized Clinical Trial

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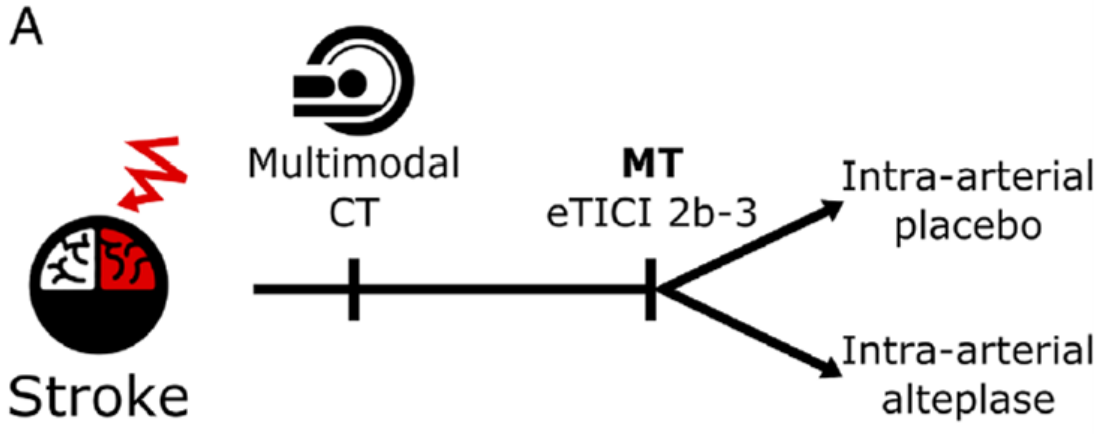

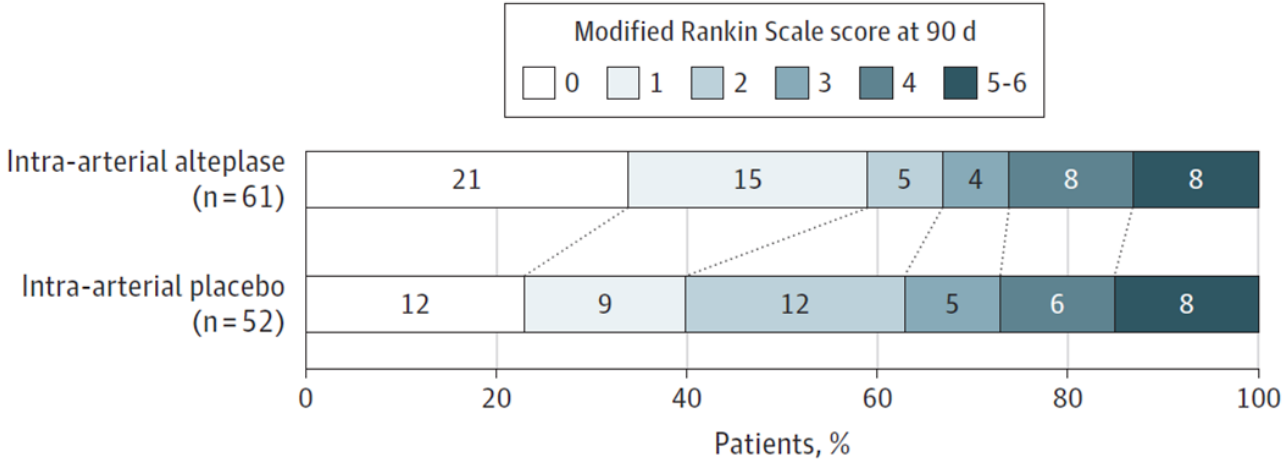

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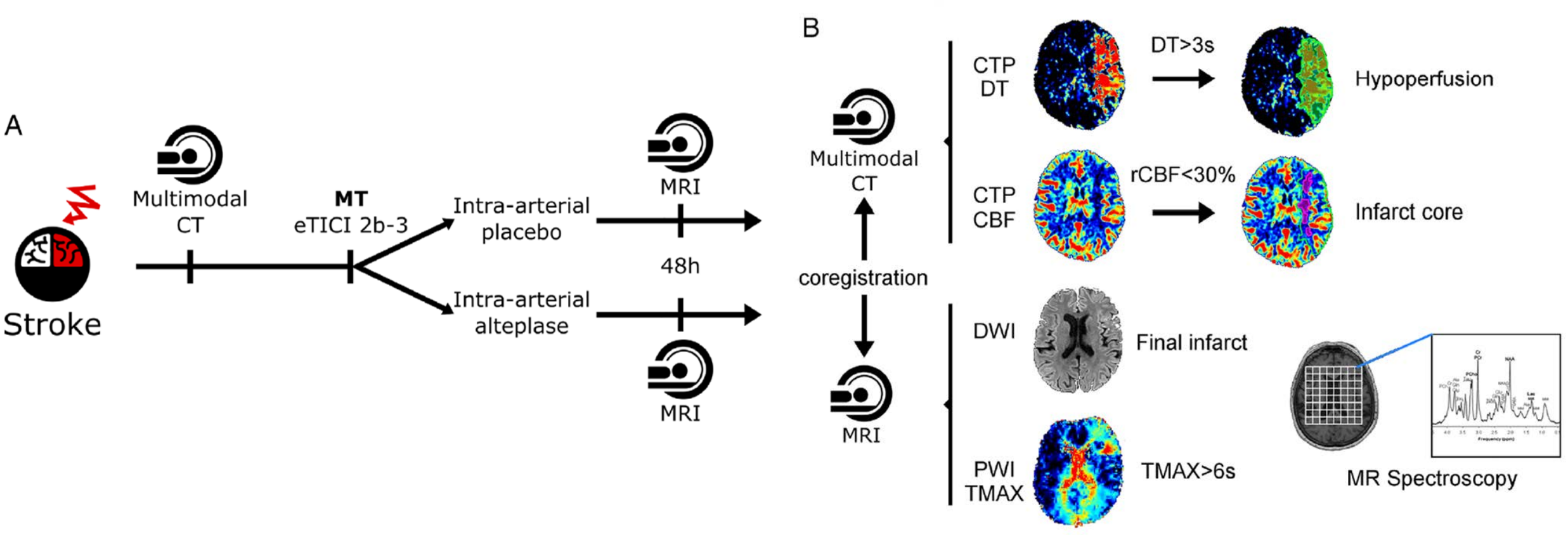
Objetivos

- Investigar por qué el tratamiento neoadyuvante con alteplasa mejora el pronóstico funcional a pesar del mismo resultado angiográfico

- Mejoría de la perfusión cerebral: mecanismo de no reflujo

- Evaluar la integridad neuronal en los diferentes grupos



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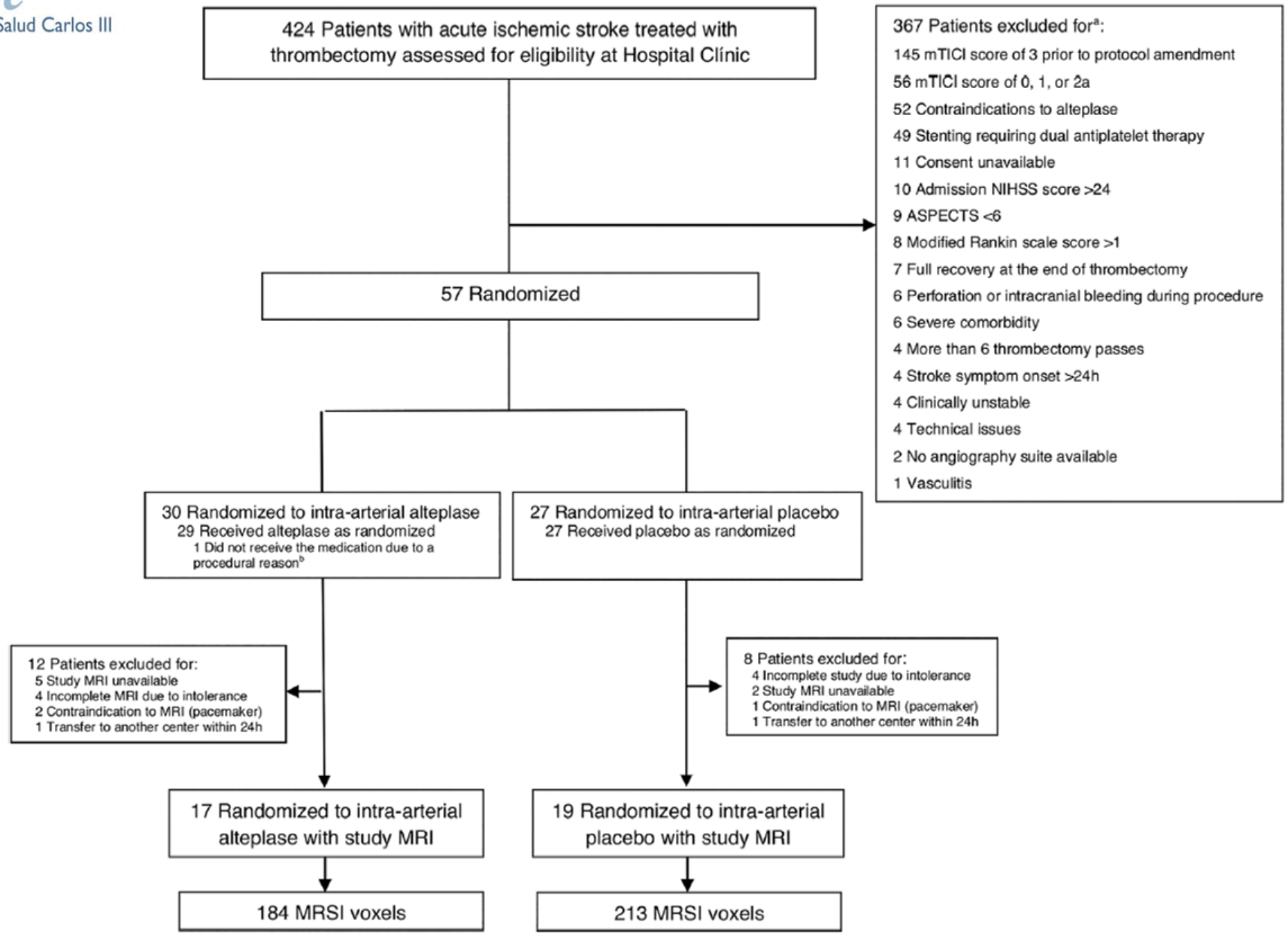

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TABLE 1. Characteristics of the Patients according to Treatment and Perfusion Pattern at Follow-up

Characteristic	Intra-Arterial Alteplase, n = 17	Intra-Arterial Placebo, n = 19	*p*
Demographics			
Age, yr, median (IQR)	71 (62–85)	75 (67–76)	0.37
Women, n (%)	10 (59%)	8 (42%)	0.32
Atrial fibrillation, n (%)	0	3 (16%)	0.09
Diabetes mellitus, n (%)	3 (18%)	4 (21%)	0.80
Hypertension, n (%)	12 (71%)	14 (74%)	0.84
Hospital admission			
SBP, mmHg, median (IQR)	135 (120–152)	135 (120–152)	0.21
DBP, mmHg, median (IQR)	72 (69–81)	73 (72–94)	0.73
Glucose, mg/dl, median (IQR)	126 (118–137)	113 (99–145)	0.40
NIHSS, median (IQR)	11 (8–18)	14 (9–18)	0.68
IV alteplase before EVT, n (%)	7 (41%)	7 (37%)	0.79
Time to randomization, min, median (IQR)	297 (201–352)	393 (301–413)	0.22
Time from CTP to MRI, h, median (IQR)	44 (24–55)	47 (29–67)	0.62
CTP admission			
Hypoperfusion, ml, median (IQR)	52.1 (39.4–76.9)	54.7 (21.5–84.6)	0.88
Core median, ml (IQR)	12.3 (9.7–17.2)	6.2 (2.1–10.3)	0.14
Mismatch, % (95% CI)	82 (72–87)	90 (83–96)	0.07
eTICI score post-thrombectomy [before randomization]			
eTICI score			0.56
eTICI 2b50	1 (6%)	1 (5%)	
eTICI 2b67	7 (41%)	6 (32%)	
eTICI 2c	2 (12%)	6 (32%)	
eTICI 3	7 (41%)	6 (32%)	

CI = confidence interval; CTP = computed tomography perfusion; DBP = diastolic blood pressure; eTICI: expanded Thrombolysis in Cerebral Infarction scale; EVT = endovascular treatment; IQR = interquartile range; IV = intravenous; MRI = magnetic resonance imaging; NIHSS = National Institutes of Health Stroke Scale; SBP = systolic blood pressure.

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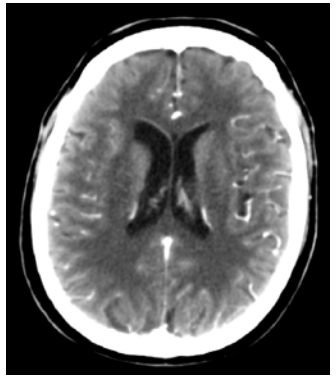
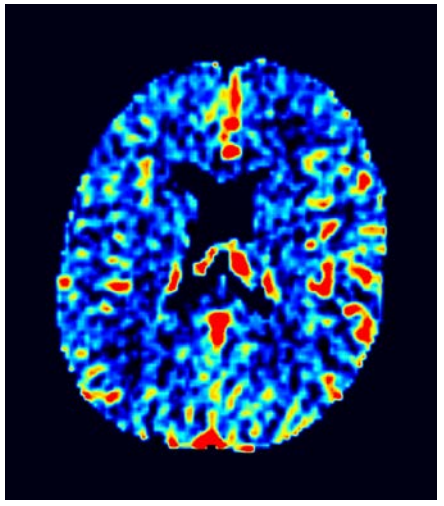
Neuroimagen - CTP



CTP



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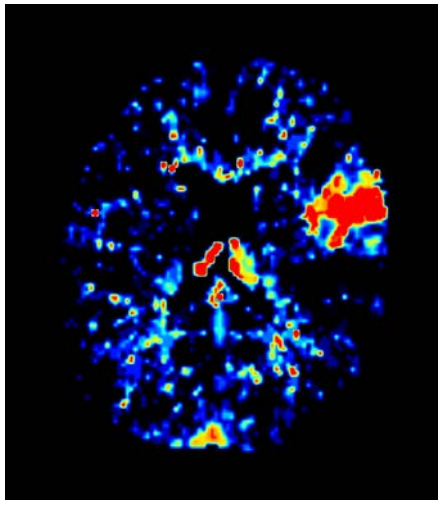

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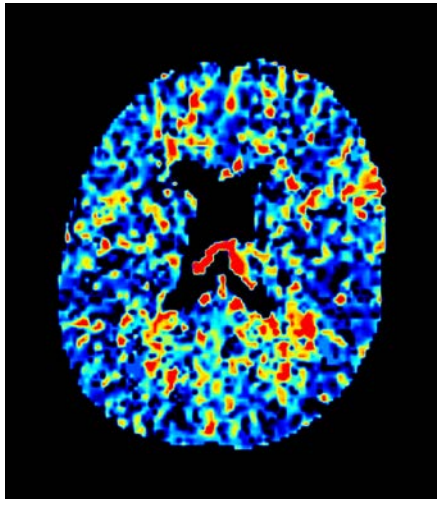

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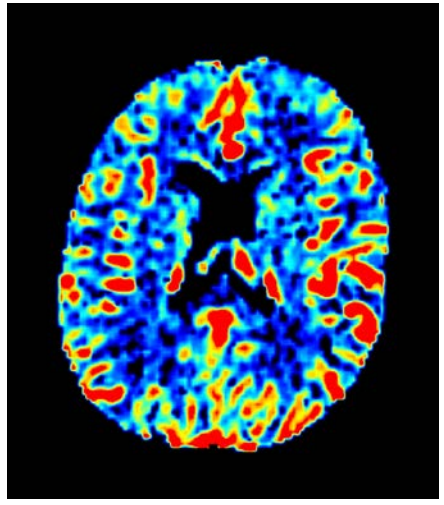
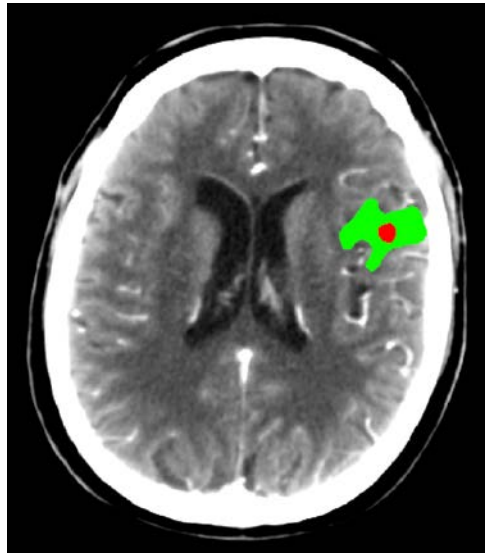


CBF

DT > 3s

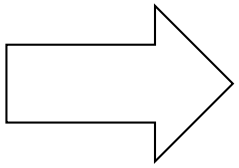
CBF < 30%



Penumbra

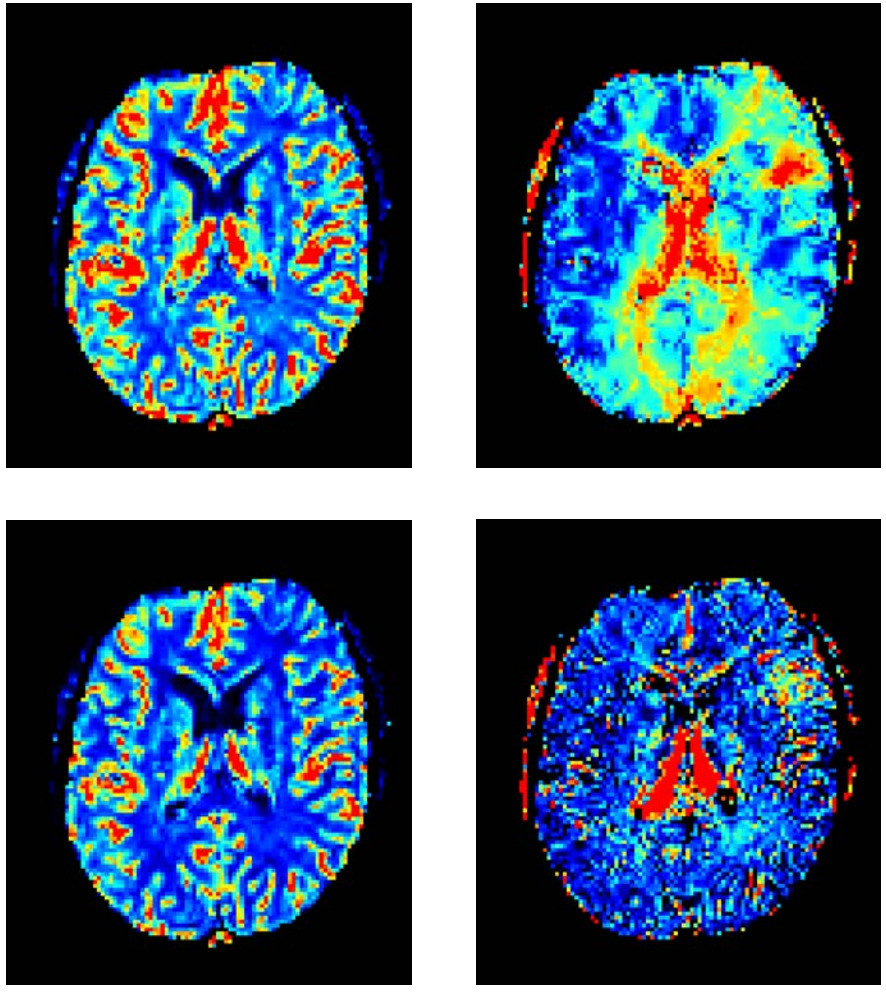
Infarct core

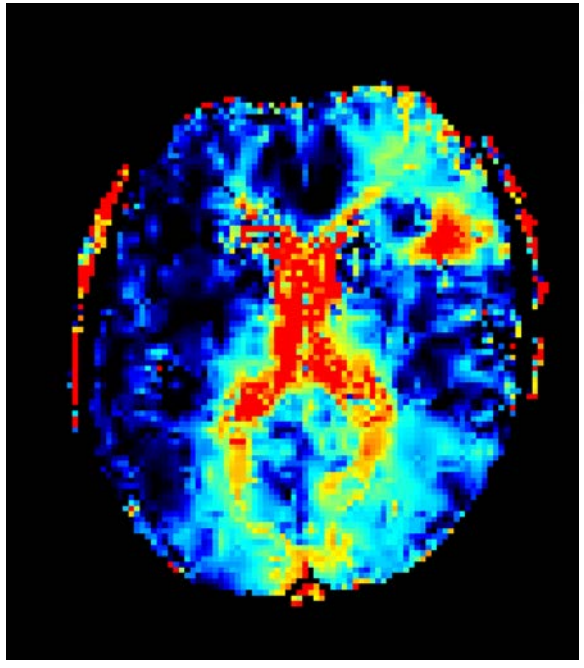
Neuroimagen - RM-difusión

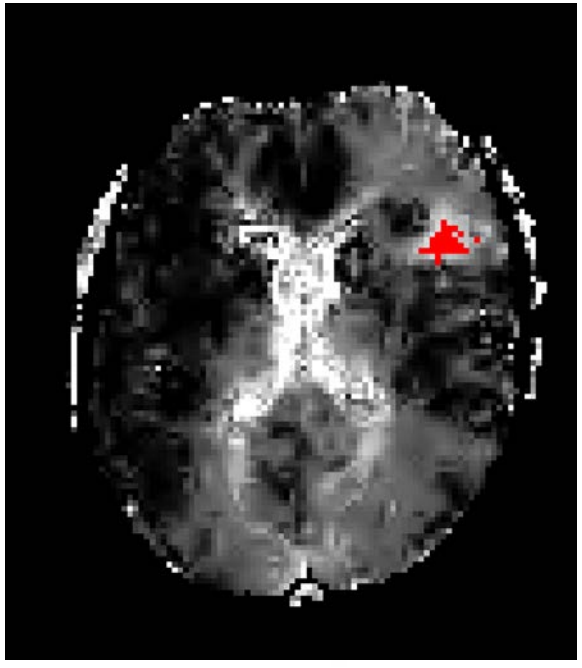


Final infarct

Neuroimagen - RM-perfusión

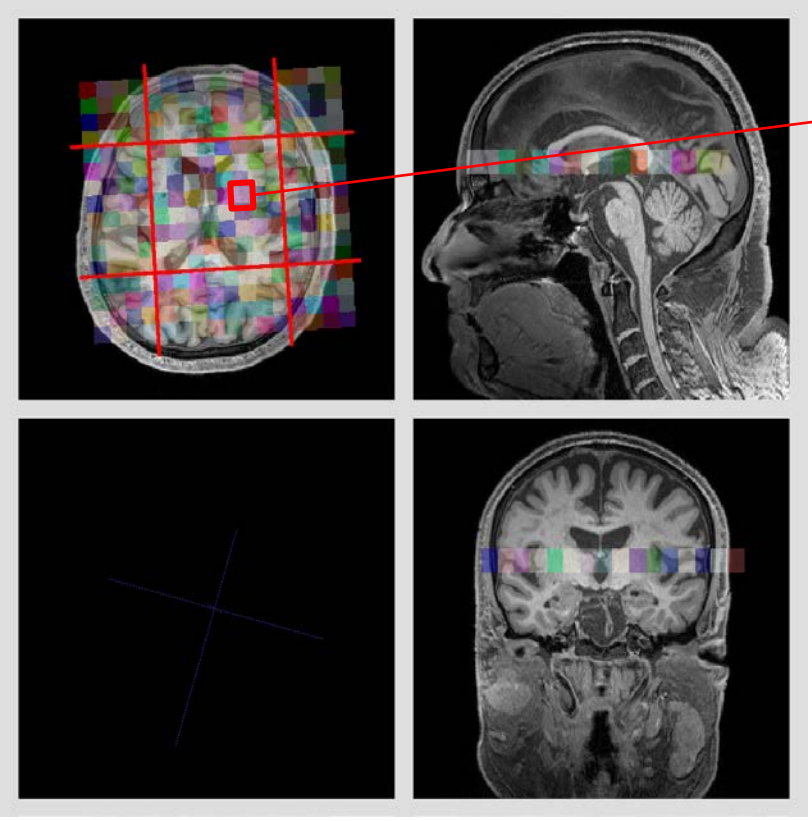




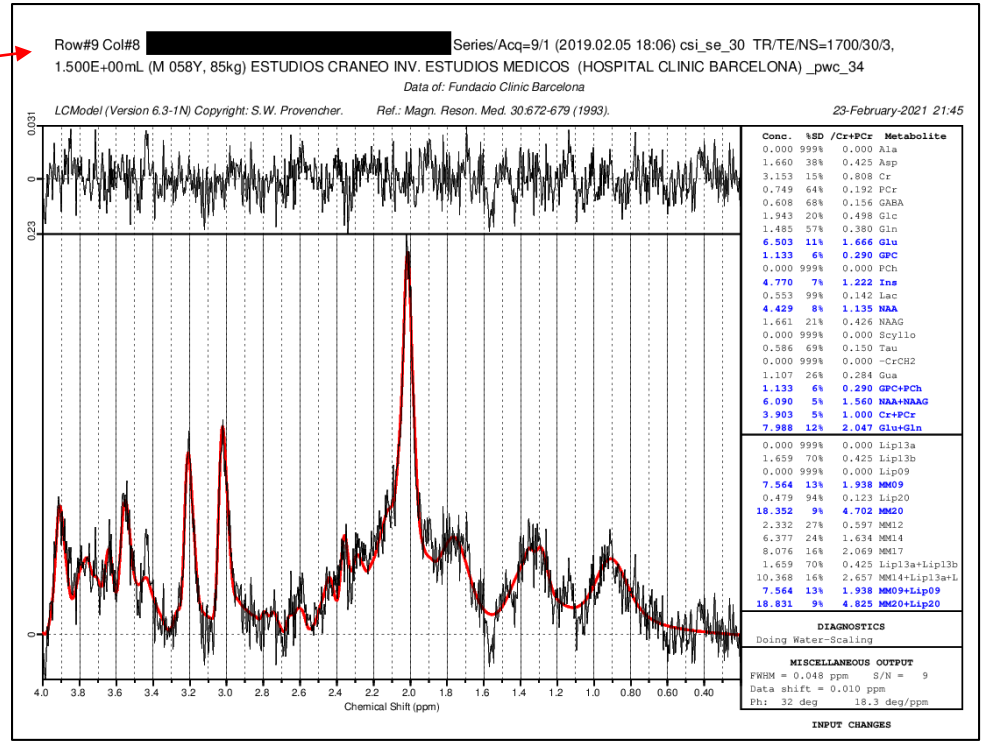


TMAX > 6s

Neuroimagen - RM espectroscópica



8x8 voxel CSI Matrix = 64 voxels



Análisis de RM-difusión

Análisis de RM-perfusión

RM espectroscópica

Análisis de RM-difusión

Análisis de RM-perfusión

RM espectroscópica

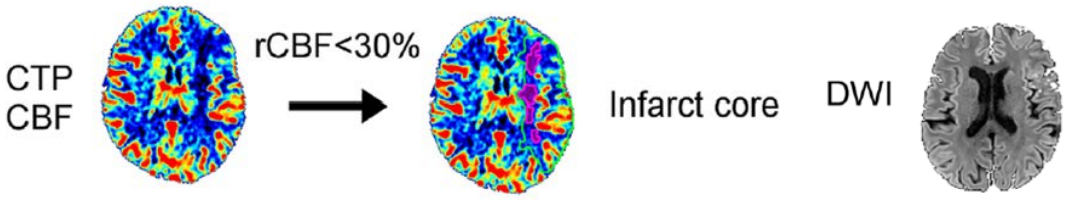


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TABLE 4. Radiological Course of the Infarction according to Treatment

	Intra-Arterial Alteplase, n = 17	Intra-Arterial Placebo, n = 19	*p*
Angiographic improvement, n (%)	0	3 (16%)	0.09
Abnormal perfusion at 48 hours, n (%)	4 (24%)	11 (58%)	0.03
TMAX > 6 volume, median (IQR)	0	0.76 (0.07–2.33)	0.04
Expanding infarction, n (%)	6 (35%)	14 (74%)	0.02
Infarct expansion ratio, median (IQR)	0.79 (0.50–1.44)	3.23 (1.79–5.73)	0.02

"Expanding infarction" indicates infarct expansion ratio > 1.
IQR = interquartile range; TMAX = time to maximum.

$$\text{IER} = \frac{\text{final infarct on DWI}}{\text{infarct core on CTP}}$$

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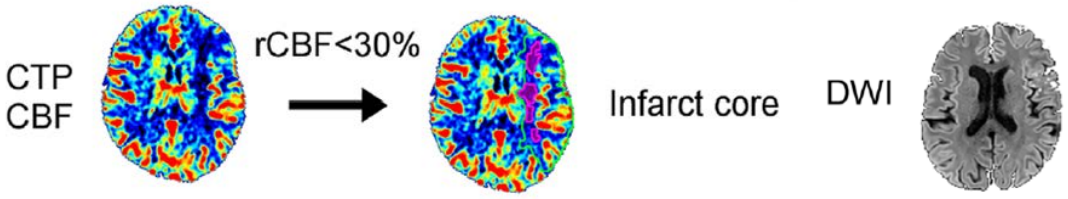

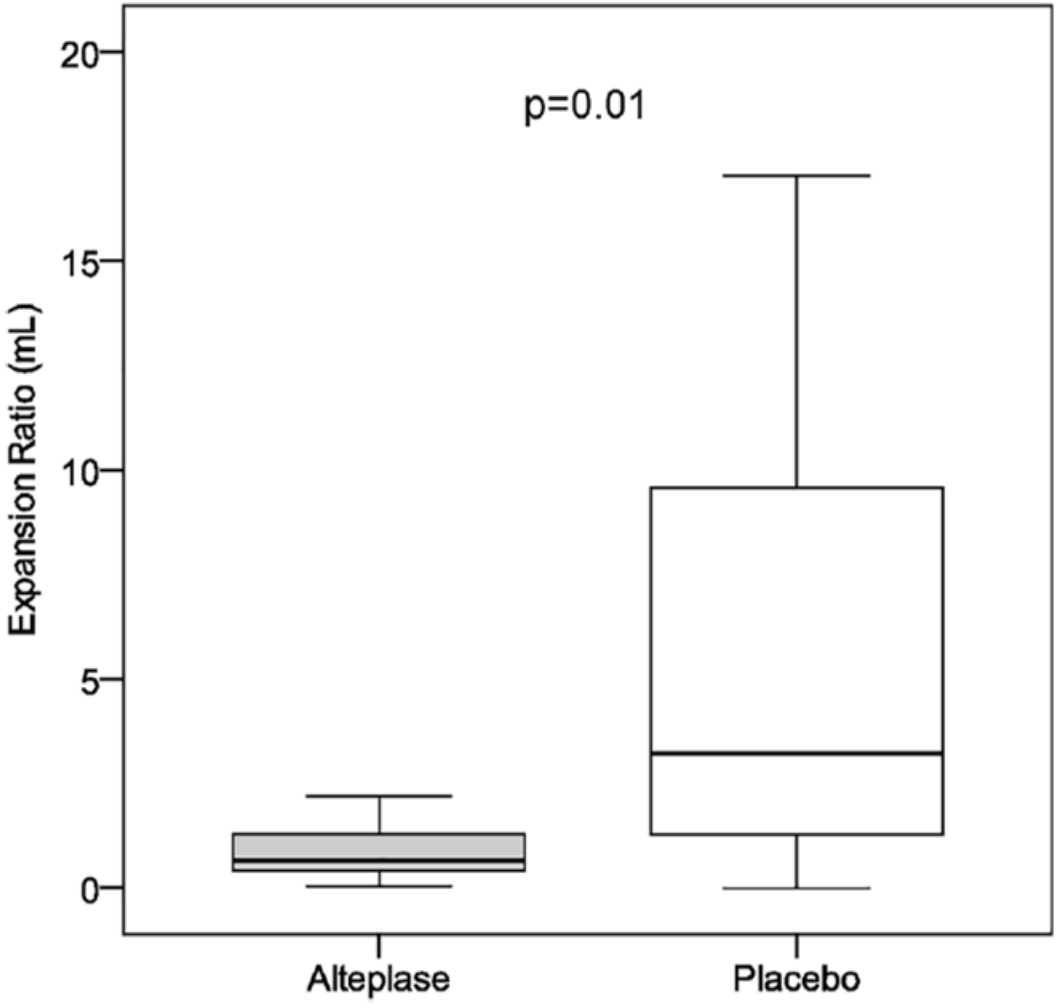

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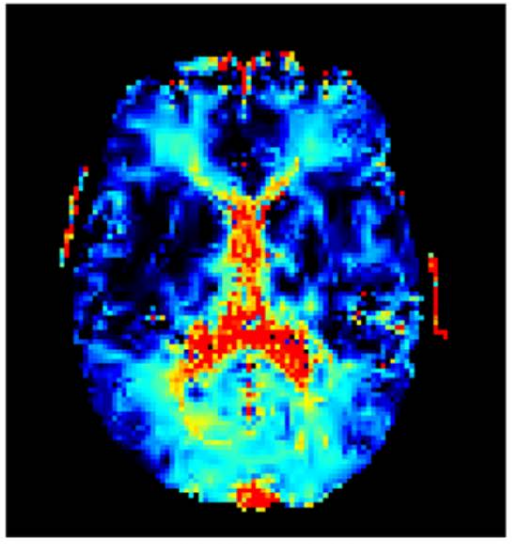
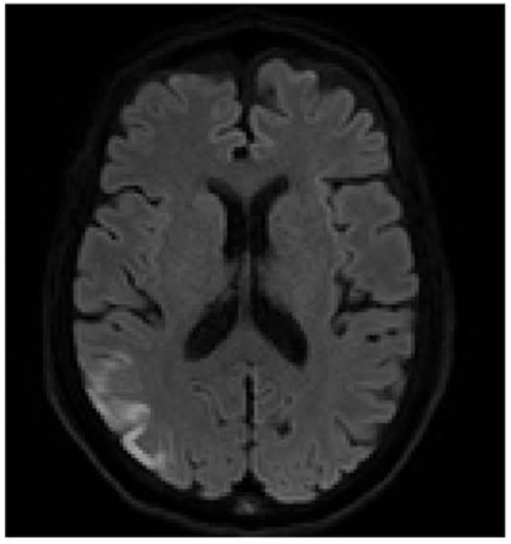
Análisis de RM-difusión

Análisis de RM-perfusión

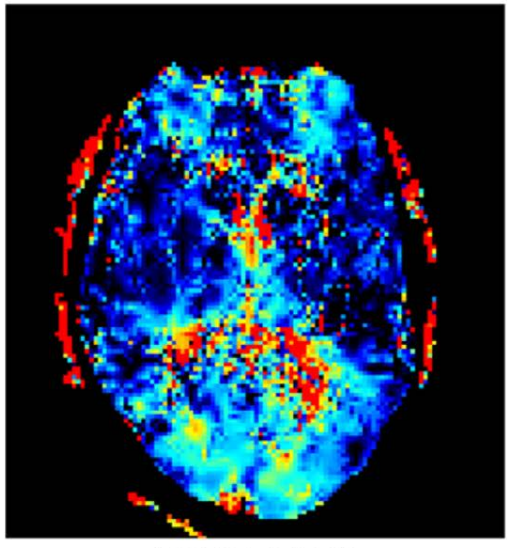
RM espectroscópica



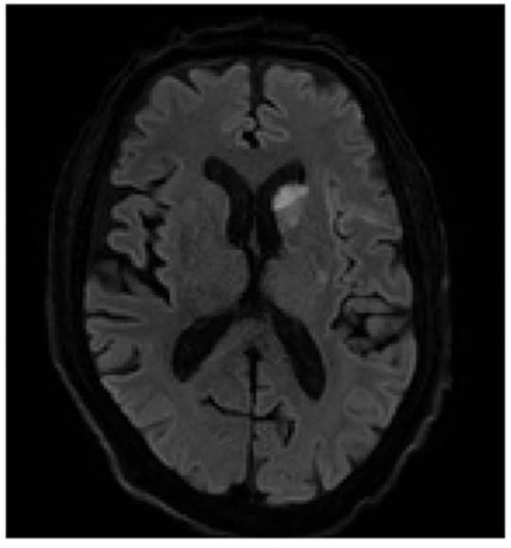
PWI TMAX



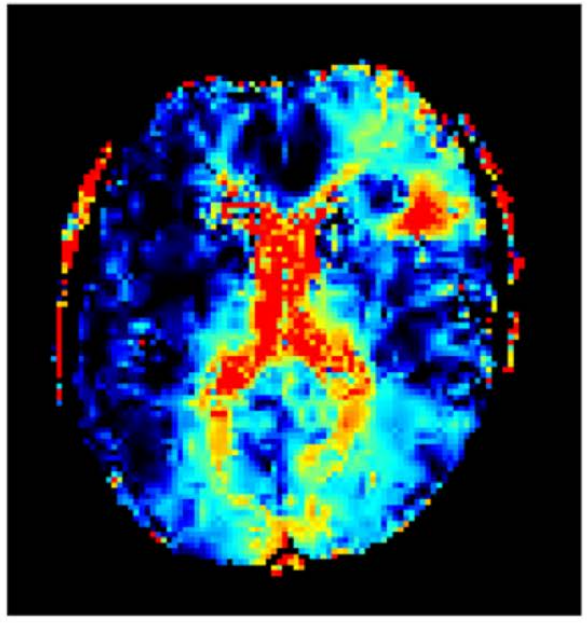
DWI



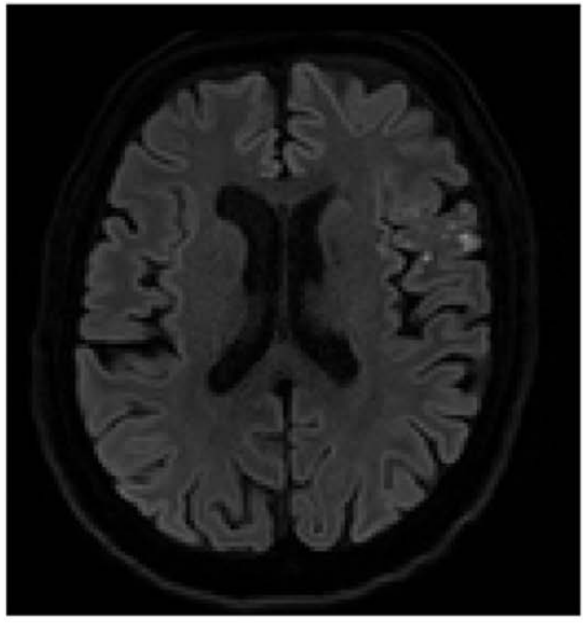
PWI TMAX



DWI



PWI TMAX



DWI

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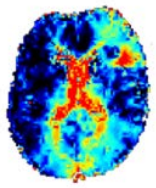

TMAX>6s

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TABLE 2. Characteristics of the Patients according to the Perfusion Pattern at 48 Hours

Characteristic	Normal Perfusion, n = 21	Abnormal Perfusion, n = 15	p
Demographics			
Age, years, median (IQR)	71 (57–77)	76 (71–86)	0.05
Women, n (%)	10 (48%)	8 (53%)	0.73
Atrial fibrillation, n (%)	1 (5%)	2 (13%)	0.35
Diabetes mellitus, n (%)	3 (14%)	4 (27%)	0.35
Hypertension, n (%)	14 (67%)	12 (80%)	0.37
Hospital admission			
SBP, mmHg, median (IQR)	138 (131–157)	145 (120–155)	0.98
DBP, mmHg, median (IQR)	73 (71–81)	71 (65–80)	0.43
Glucose, mg/dl, median (IQR)	115 (98–134)	140 (118–166)	0.01
NIHSS, median (IQR)	9 (7–19)	15 (11–20)	0.55
IV alteplase before EVT, n (%)	7 (33%)	7 (47%)	0.41
Time to randomization, min, median (IQR)	315 (204–518)	393 (297–450)	0.46
CTP admission			
Hypoperfusion, ml, median (IQR)	50.5 (34.1–83.8)	55.7 (27.2–93.5)	0.71
Core median, ml (IQR)	10.0 (7.1–14.7)	6.2 (2.5–12.5)	0.59
Mismatch, % (95% CI)	86 (72–96)	88 (81–94)	0.73
Final eTICI score			
eTICI score			0.13
eTICI 2b50	0 (0%)	2 (100%)	
eTICI 2b67	6 (46%)	7 (54%)	
eTICI 2c	5 (63%)	3 (38%)	
eTICI 3	10 (77%)	3 (23%)	
Infarct course at 48 hours			
Infarct expansion ratio, median (IQR)	0.7 (0.5–2.1)	3.2 (1.8–4.3)	0.06
Infarct volume, ml, median (IQR)	5.7 (4.9–12.2)	18.6 (7.7–32.1)	0.02

CI = confidence interval; CTP = computed tomography perfusion; DBP = diastolic blood pressure; eTICI: expanded Thrombolysis in Cerebral Infarction scale; EVT = endovascular treatment; IQR = interquartile range; IV = intravenous; NIHSS = National Institutes of Health Stroke Scale; SBP = systolic blood pressure.

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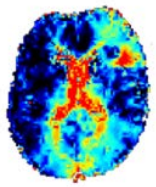

TMAX>6s

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TABLE 3. Clinical Association of the Perfusion Patterns at Follow-up

	Normal Perfusion, n = 21	Abnormal perfusion, n = 15	*p*
mRS score at day 90			
mRS 0–1, n (%)	18 (86%)	9 (60%)	0.07[a]
mRS 0–2—n (%)	21 (100%)	10 (67%)	0.004
Barthel Index at day 90			
Barthel Index > 95–100, n (%)	20 (95%)	7 (47%)	0.001
NIHSS course, median (IQR)			
Baseline	9 (7–19)	15 (11–20)	0.56
24 h	0	6 (3–13)	0.001
48 h	0	3 (2–7)	0.001
Day 5–7	0	2 (1–7)	0.005
Day 90	0	0 (0-2)	0.01

[a]The association between abnormal perfusion pattern at 48 hours and mRS 0–1 at day 90 was independent of the final expanded Thrombolysis in Cerebral Infarction score (odds ratio = 0.15, 95% confidence interval = 0.03–0.93, $p = 0.04$).

IQR = interquartile range; mRS = modified Rankin Scale; NIHSS = National Institutes of Health Stroke Scale.

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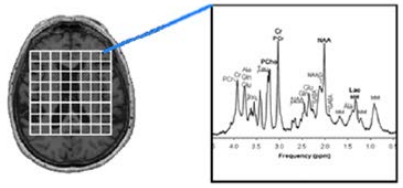

MR Spectroscopy

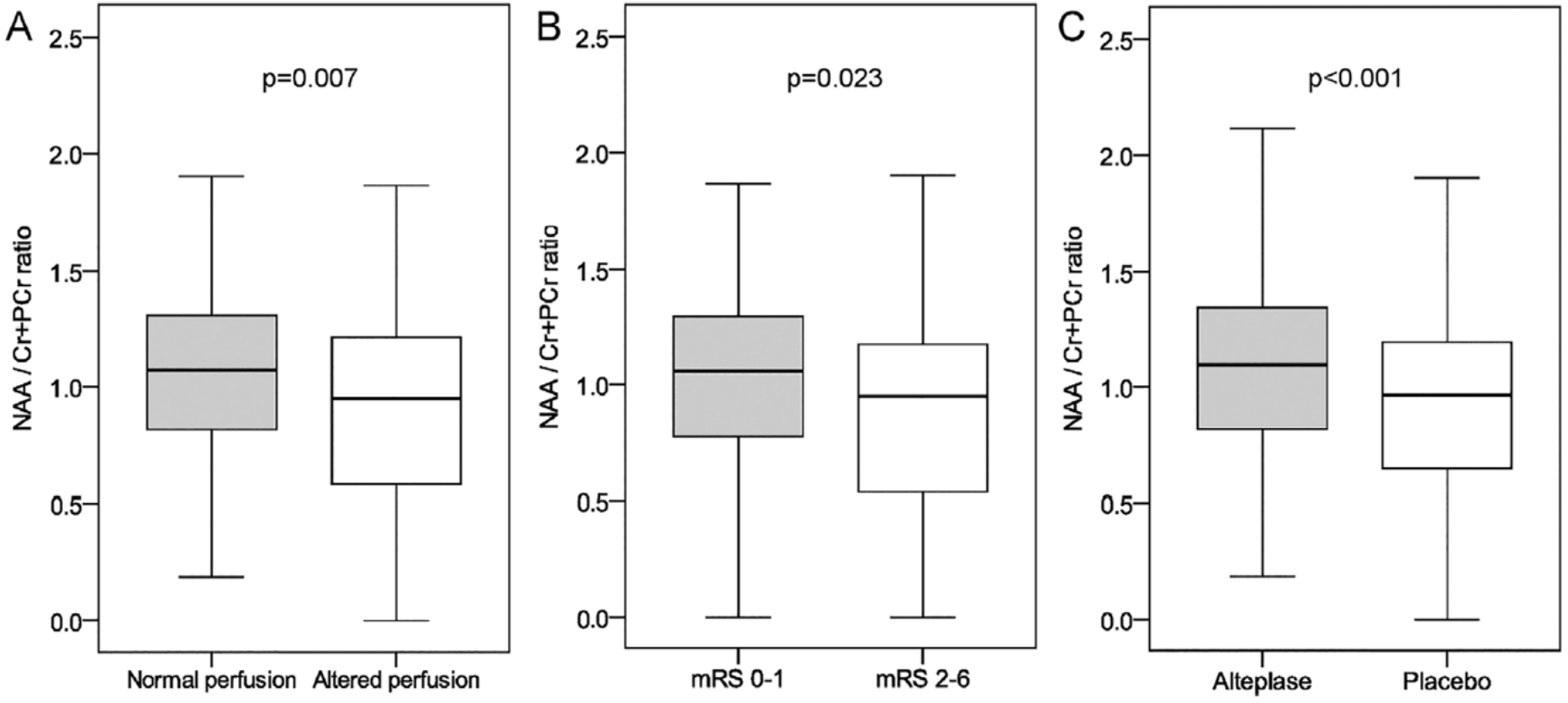

FIGURE 5: N-Acetylaspartate (NAA) peaks according to the perfusion pattern, functional outcome, and study treatment (boxes indicate 25–75% interquartile range [IQR]; central horizontal bars indicate median; outer horizontal bars indicate 10–90% IQR). mRS = modified Rankin Scale.

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Conclusiones

- La fibrinolisis post-trombectomía mejora de forma significativa la perfusión en RM a las 48 horas
- Esta mejoría se produce independientemente de los resultados angiográficos
- La fibrinolisis post-trombectomía se asocia a un menor índice de crecimiento del infarto
- El uso de alteplasa intraarterial se asocia a mayores picos de NAA consistente con un aumento de la densidad neuronal, lo que se relaciona con el incremento de perfusión microvascular y mejor resultado funcional

Más allá...

- CHOICE-2
- Replicar los resultados: colaboración
- Método de evaluación de fármacos neuroprotectores
- Otros escenarios: pronóstico post-tratamiento, daño por reperfusión, lesiones cerebrales extensas...


Gracias