

Nuove frontiere nel campo del trattamento della fase acuta dello stroke

Maurizio Paciaroni



DISCLOSURES

Maurizio Paciaroni has served in the last 5 years on the speakers' bureaus of:

- Bayer
- Boehringer Ingelheim
- Bristol-Myers Squibb
- Daiichi Sankyo
- Pfizer
- Sanofi Aventis

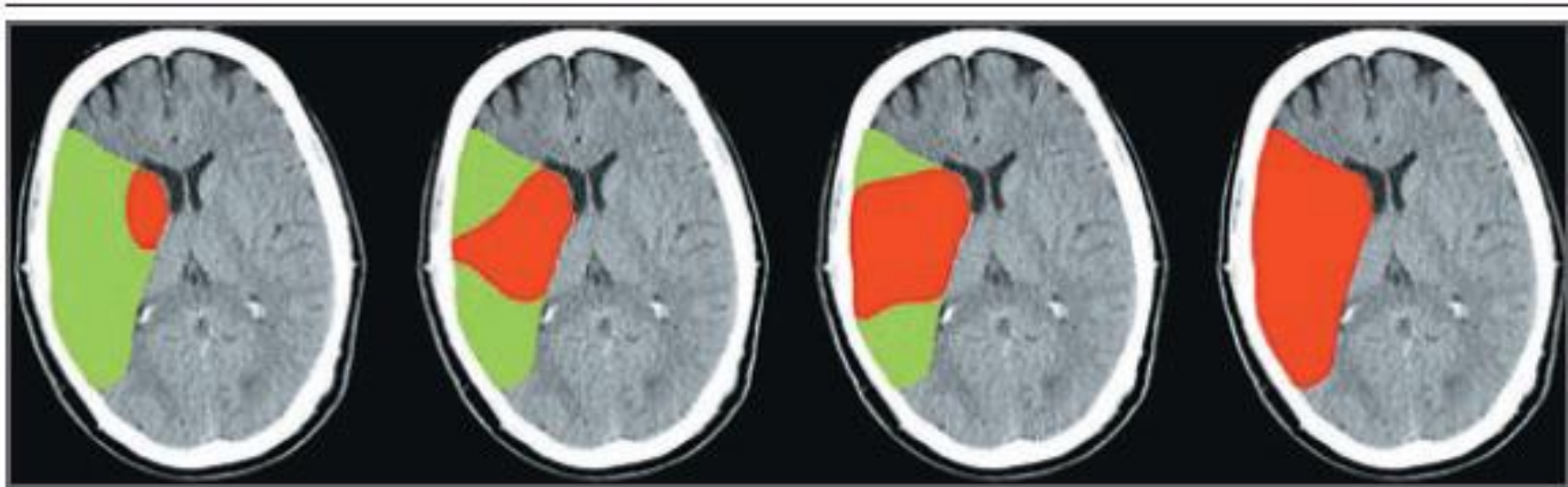
Highlights

- Reperfusion therapy
- Early secondary prevention
- Early worsening after a stroke

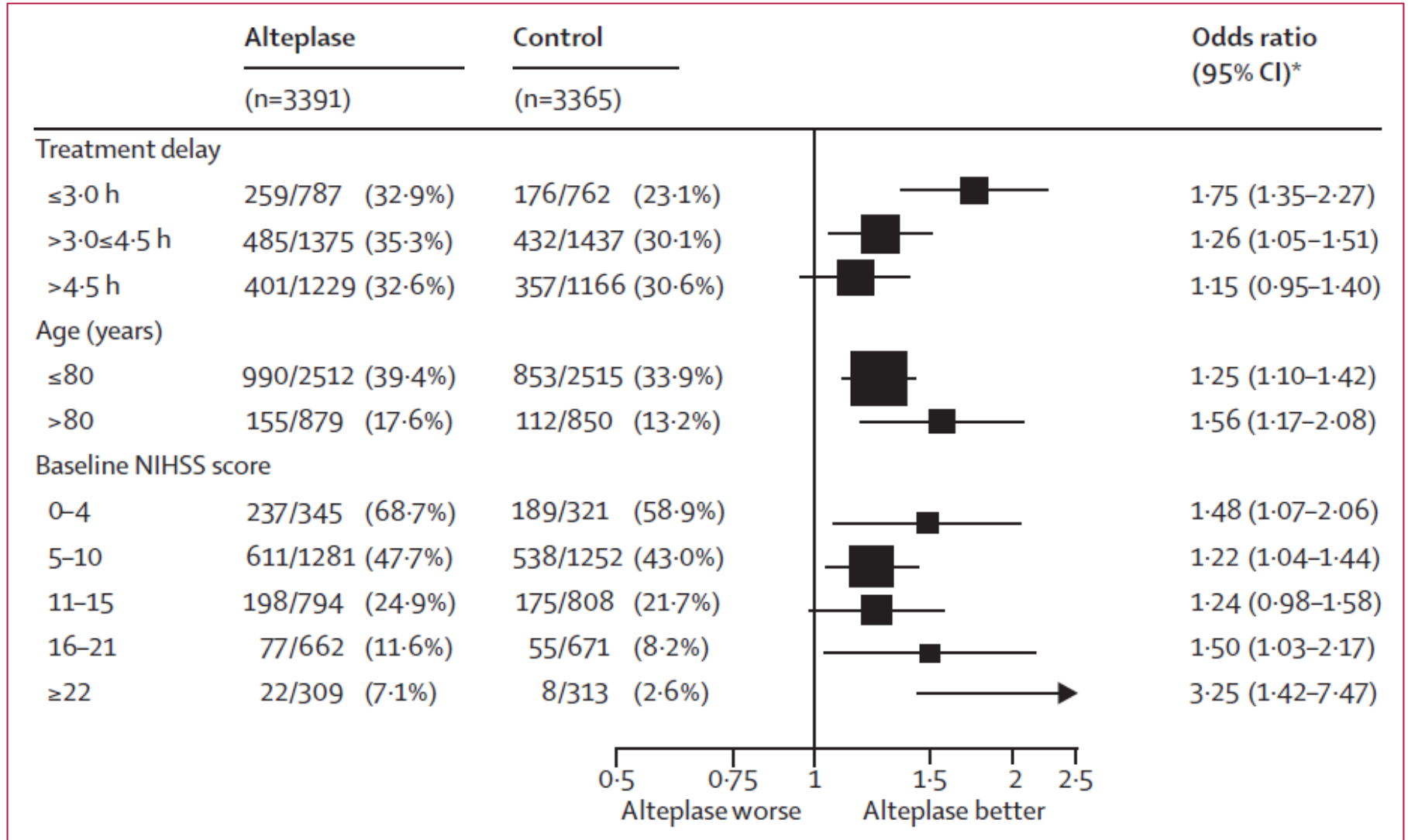
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Reperfusion therapy



Effect of rtPA on good stroke outcome (mRS 0–1)



L'rt-PA e.v. (0,9 mg/kg, dose massima 90 mg, il 10% della dose in bolo, il rimanente in infusione di 60 minuti) è indicato entro 4 ore e 30 minuti dall'esordio di un ictus ischemico



Trombectomy Intra-arteriosa

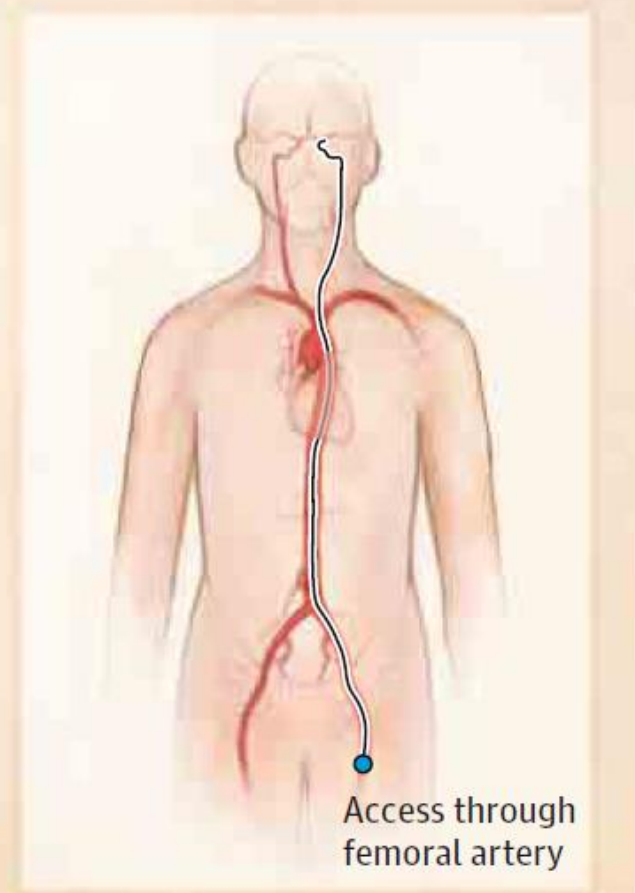
Coil retriever



Aspiration device



Stent retriever



Access through femoral artery

Design of recently published RCT on EVT

Clinical trial Control	Time window OTR time	Trial end	Proven occlusion	Ischaemic penumbra	IV alteplase (%)	OTG time	Stent-retriever	Outcome variable
MR CLEAN (n=500) IV alteplase	6.0h 204 min	Ended	ICA, M1, M2, A1, A2	NA	rt-PA failure 89%	260 min	81%	mRS at 90d (shift)
ESCAPE (n=316) BMT	12.0h 169 min	Halted	ICA, M1	ASPECT 6-10 Good collaterals	Bridging 75%	185 min	86%	mRS at 90d (shift)
EXTEND IA (n= 70) IV alteplase	4.5h 157 min	Halted	ICA, M1, M2	CTP or MRI Tmax 6sec Core <70mL	Bridging 100%	210 min	100%	24h reperfusion 3 days NIHSS
SWIFT PRIME (n=196) Iv alteplase	6h 188 min	Halted	ICA, M1	ASPECT 6-10*	Bridging 100%	224 min	100%	mRS at 90d (shift)
REVASCAT (n=206) BMT	8.0h 223 min	Halted after 1 st interim	ICA, M1	ASPECT 6-10	rt-PA failure (30') 73%	269 min	100%	mRS at 90d (shift)

- 1 - Berkhemer OA et al. N Engl J Med 2015;372:11-20.
- 2 - Goyal M et al. N Engl J Med 2015; ePub February 11
- 3 - Campbell BCV et al. N Engl J Med 2015; ePub February 11
- 4 - Saver J et al. N Engl J Med 2015, ePub April 17
- 5 – Jovin T et al. N Engl J Med 2015, ePub April 17

OTR: median time from onset to randomisation; OTG: median time from onset to groin puncture; mRS, modified Rankin scale; BMT: Best medical therapy (includes IV alteplase if eligible); RCT, randomised controlled trial; EVT, endovascular therapy; ICA, internal carotid artery; CTP, computer tomography perfusion
* MRI or CTP mismatch >1.8 in the first 71 patients

Objective: Good outcome vs therapy effect

	mRS 0-2 MT	mRS 0-2 Control	ARR	NNT (mRS 0-2)
MR Clean	33%	19%	14%	7
REVASCAT	44%	28%	16%	6
ESCAPE	53%	29%	24%	4
SWIFT-PRIME	60%	35%	25%	4
EXTEND IA	71%	40%	31%	3

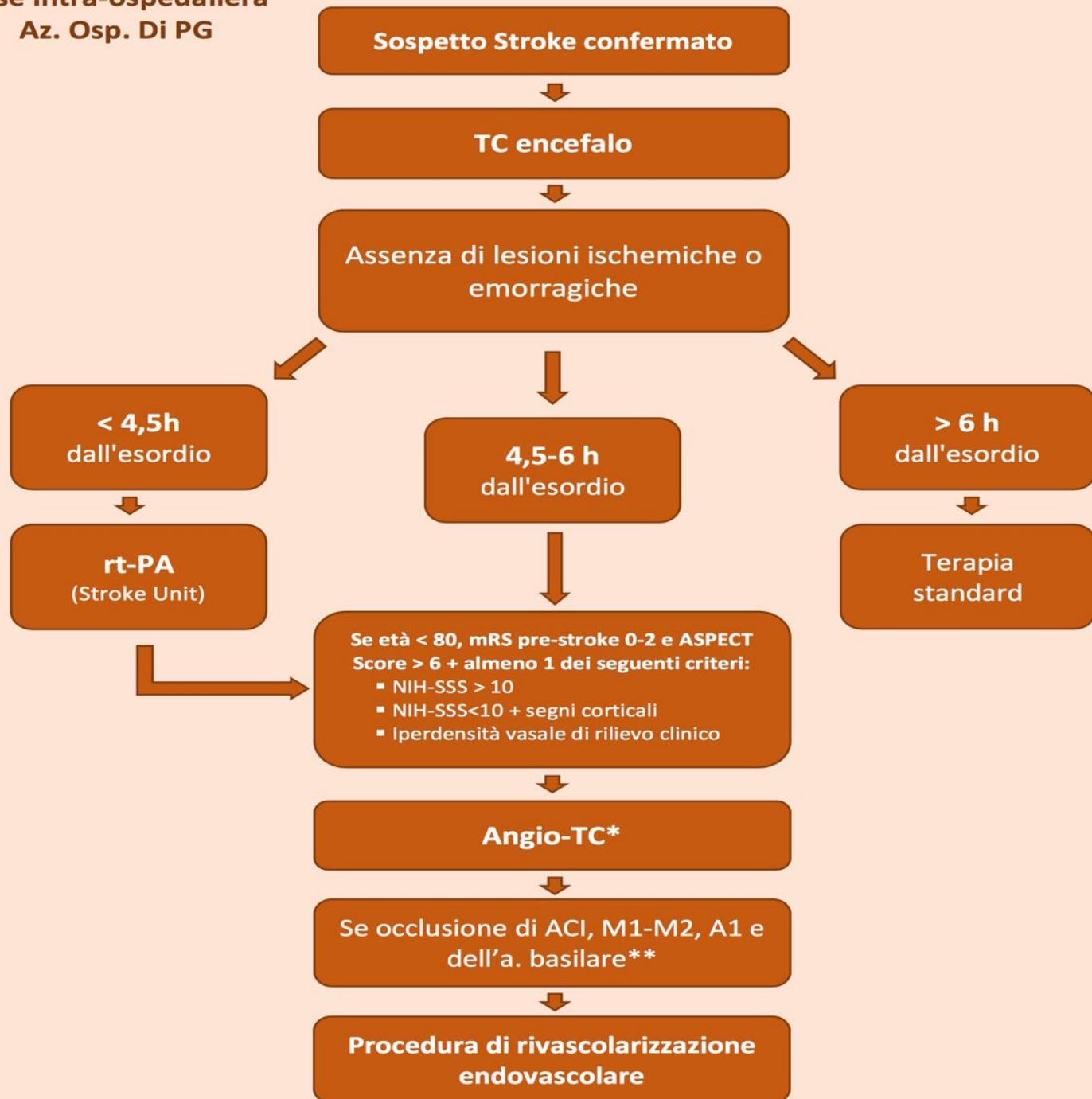
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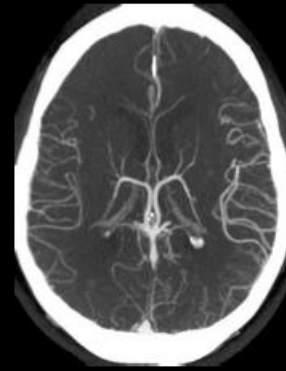
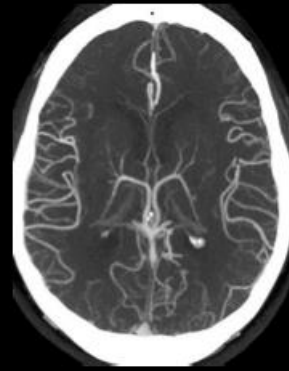
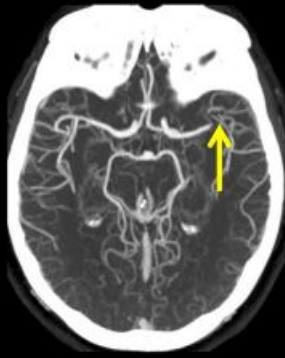
Site of Occlusion

Phase 1

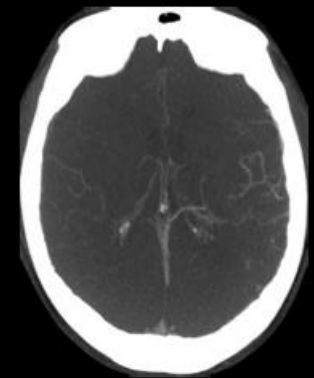
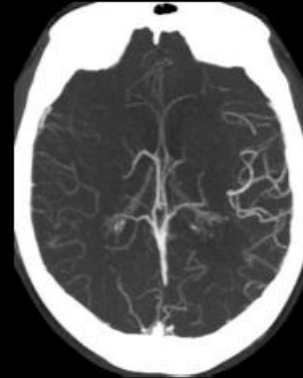
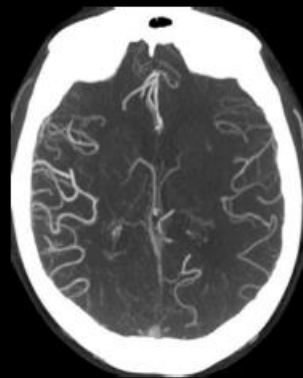
Phase 2

Phase 3

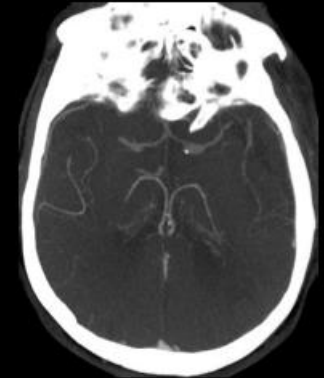
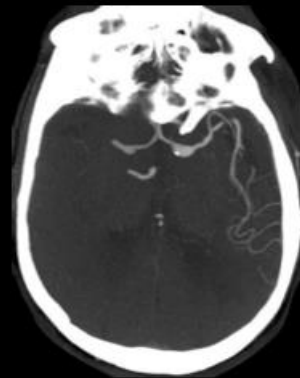
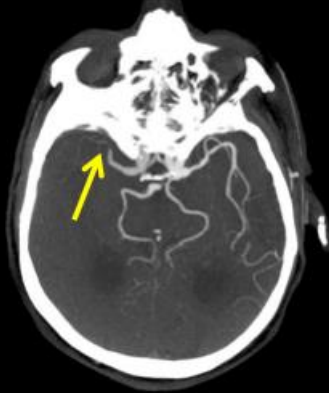
Good
collaterals



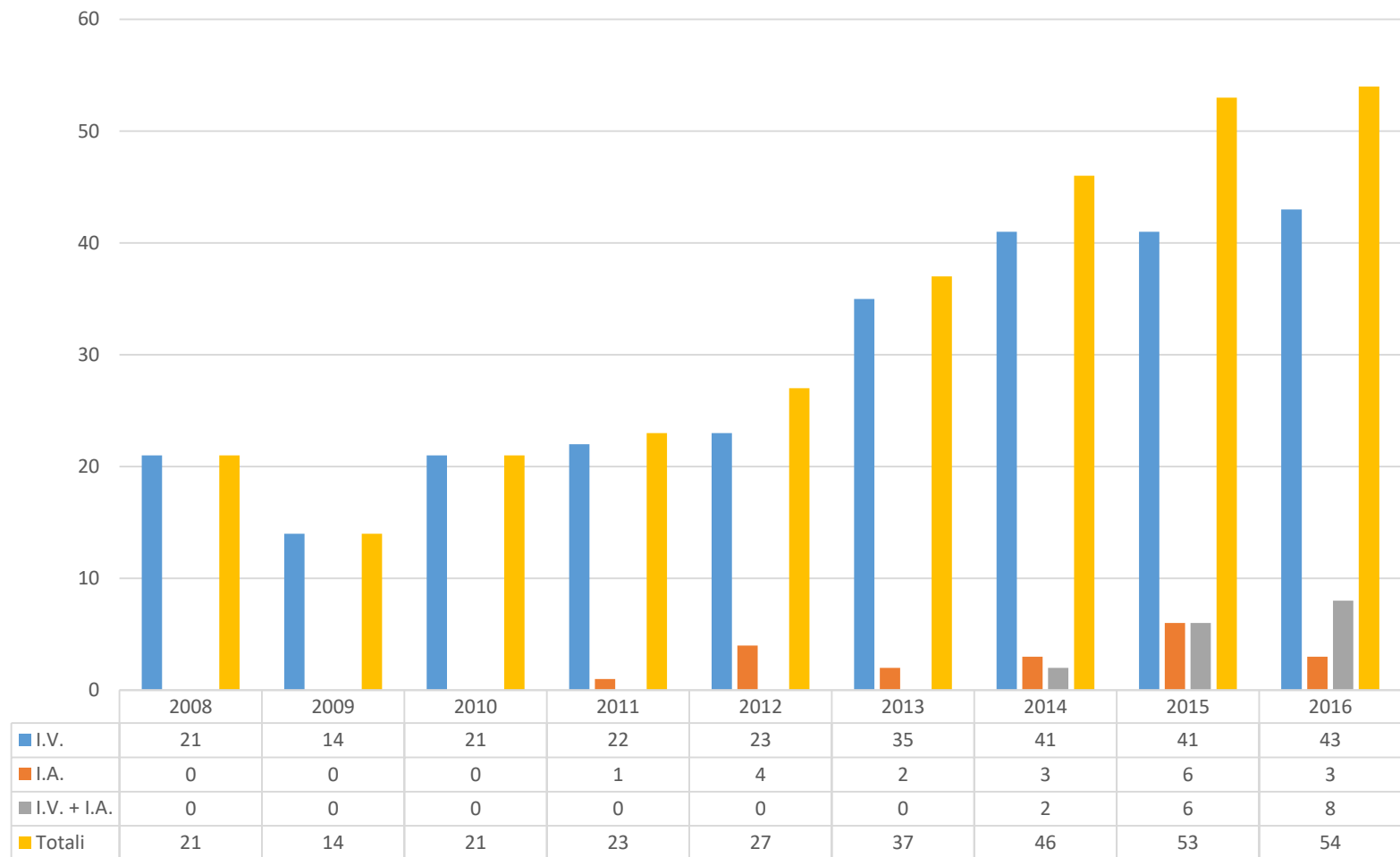
Intermediate
collaterals



Poor
collaterals



Reperfusion treatments: Perugia Stroke Unit



I.V. trombolisi endovena

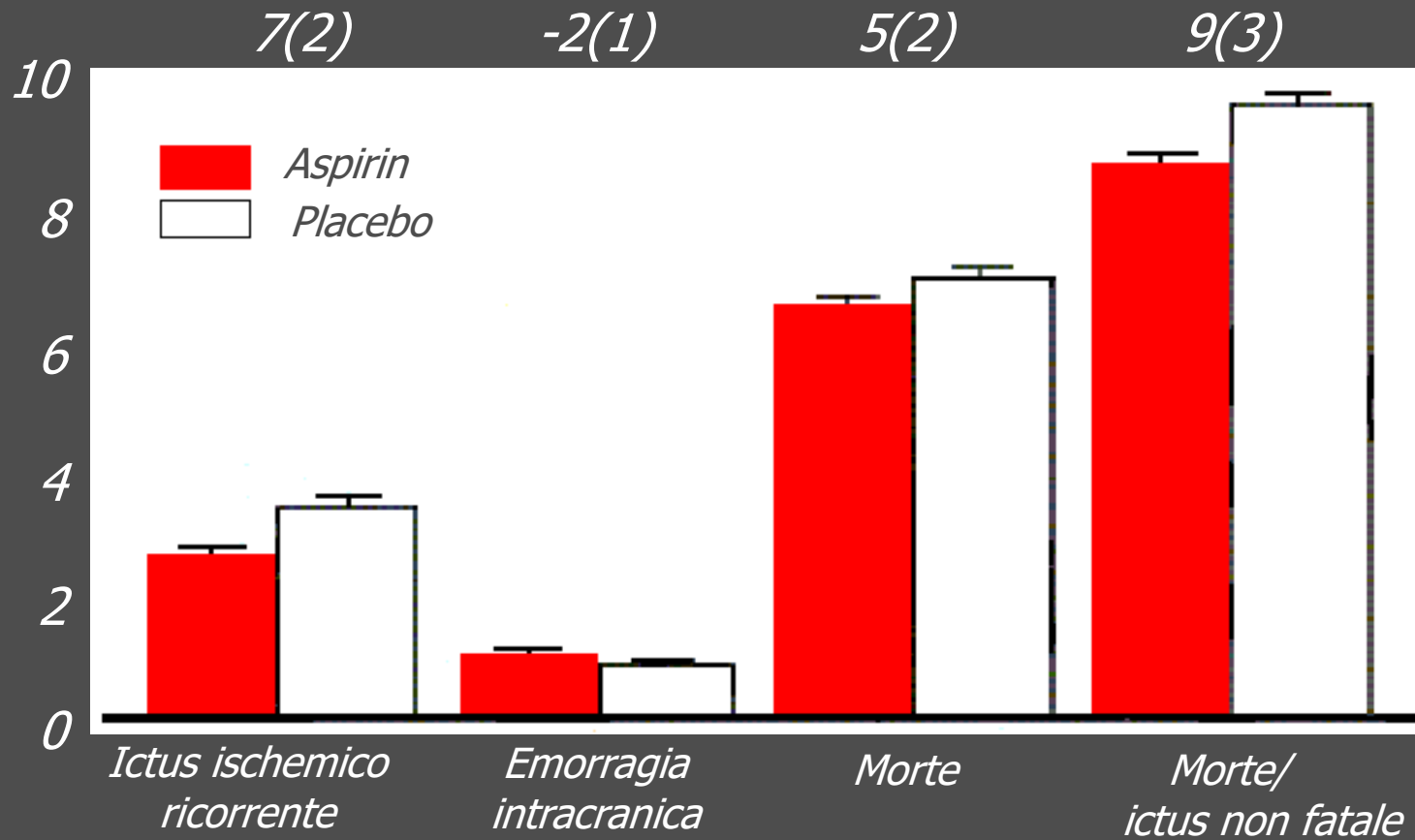
I.A. trombectomia meccanica (Dr. Hamam)

Highlights

- Reperfusion therapy
- **Early secondary prevention**
- Early worsening after a stroke

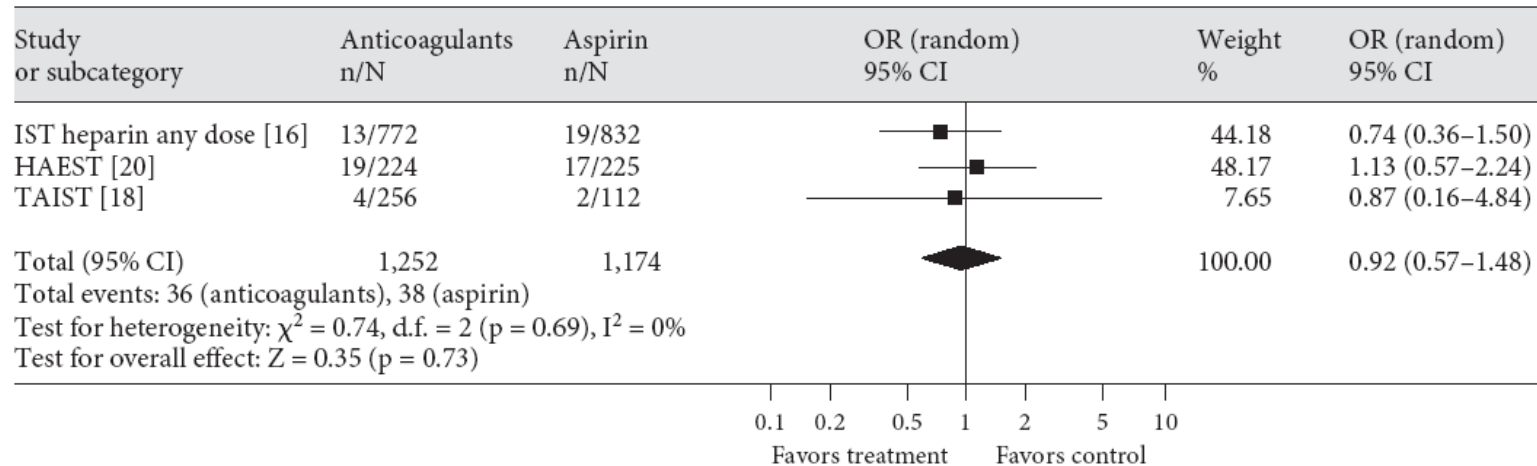
MAST-I, IST, CAST: Aspirin

Effetto per 1000 pazienti trattati

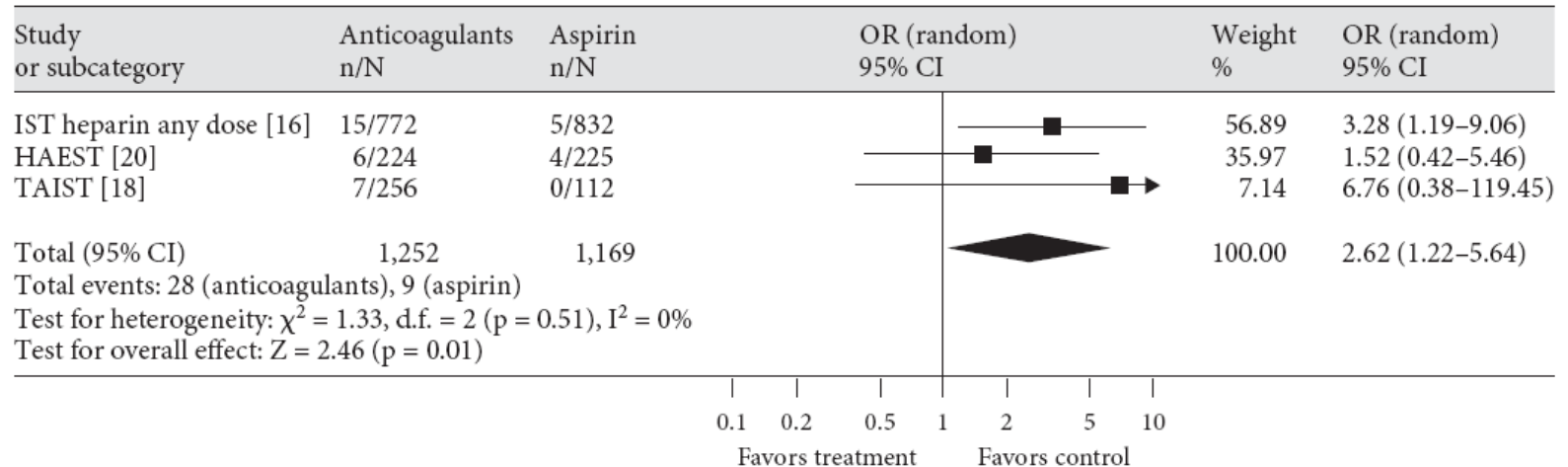


Anticoagulants in acute cardioembolic stroke

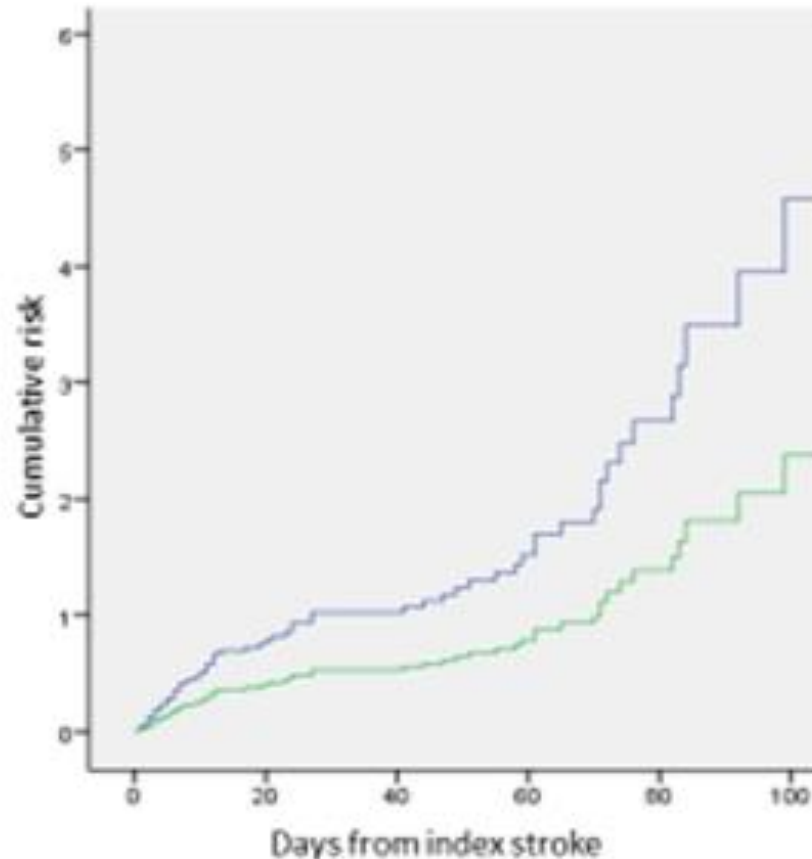
b Outcome: recurrent stroke (anticoagulants vs. aspirin)



b Outcome: hemorrhagic stroke (anticoagulants vs. aspirin)



Early Recurrence and cerebral bleeding in patients with acute ischemic stroke and Atrial Fibrillation: effect of anticoagulation and its timing. The (RAF) study
Combined endpoint: Ischemic recurrence and HT



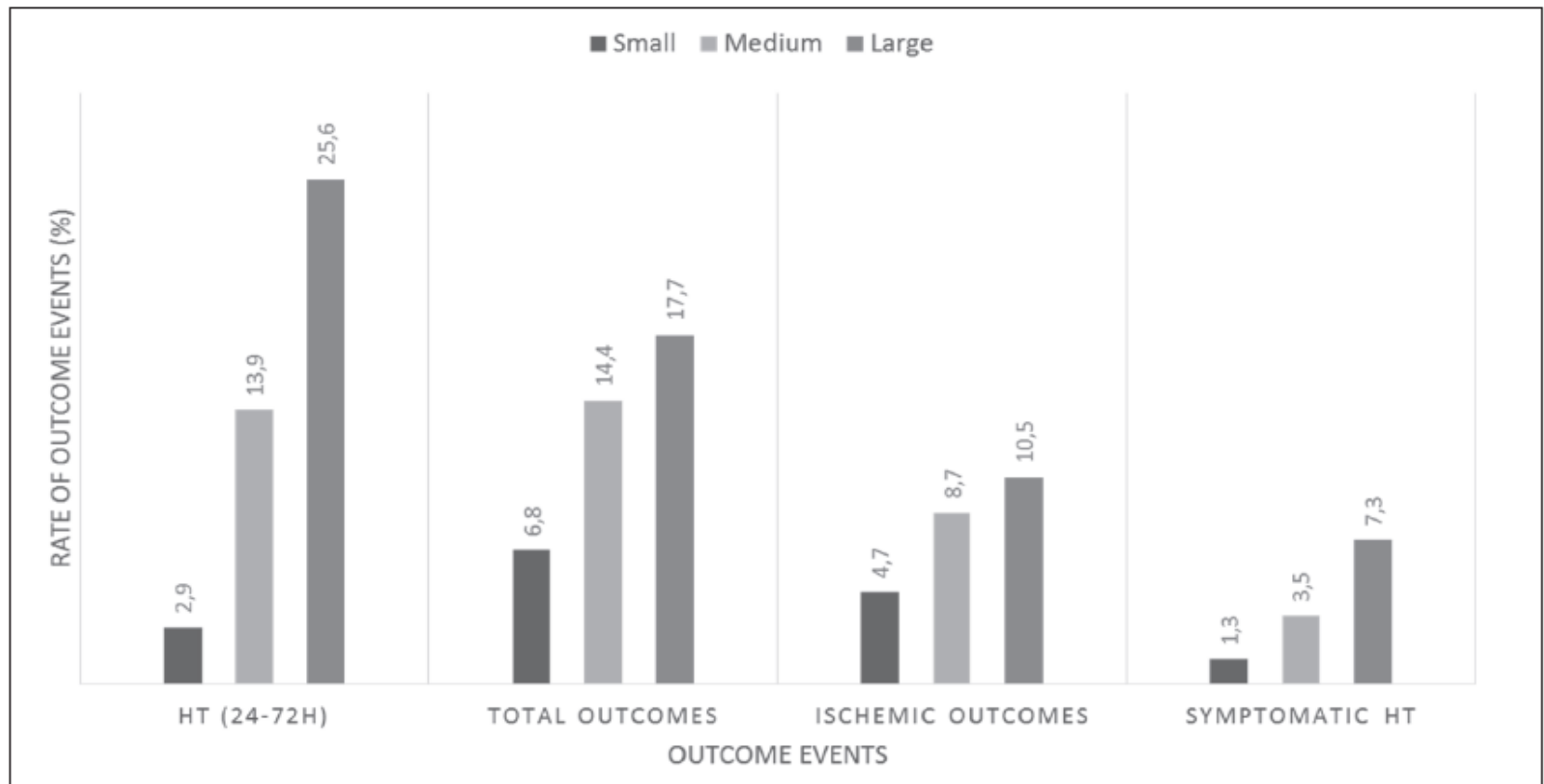
Green: anticoagulation between 4-14 days from stroke onset
Blue: other treated patients

HR=0.53 (0.30-0.93), p=0.025

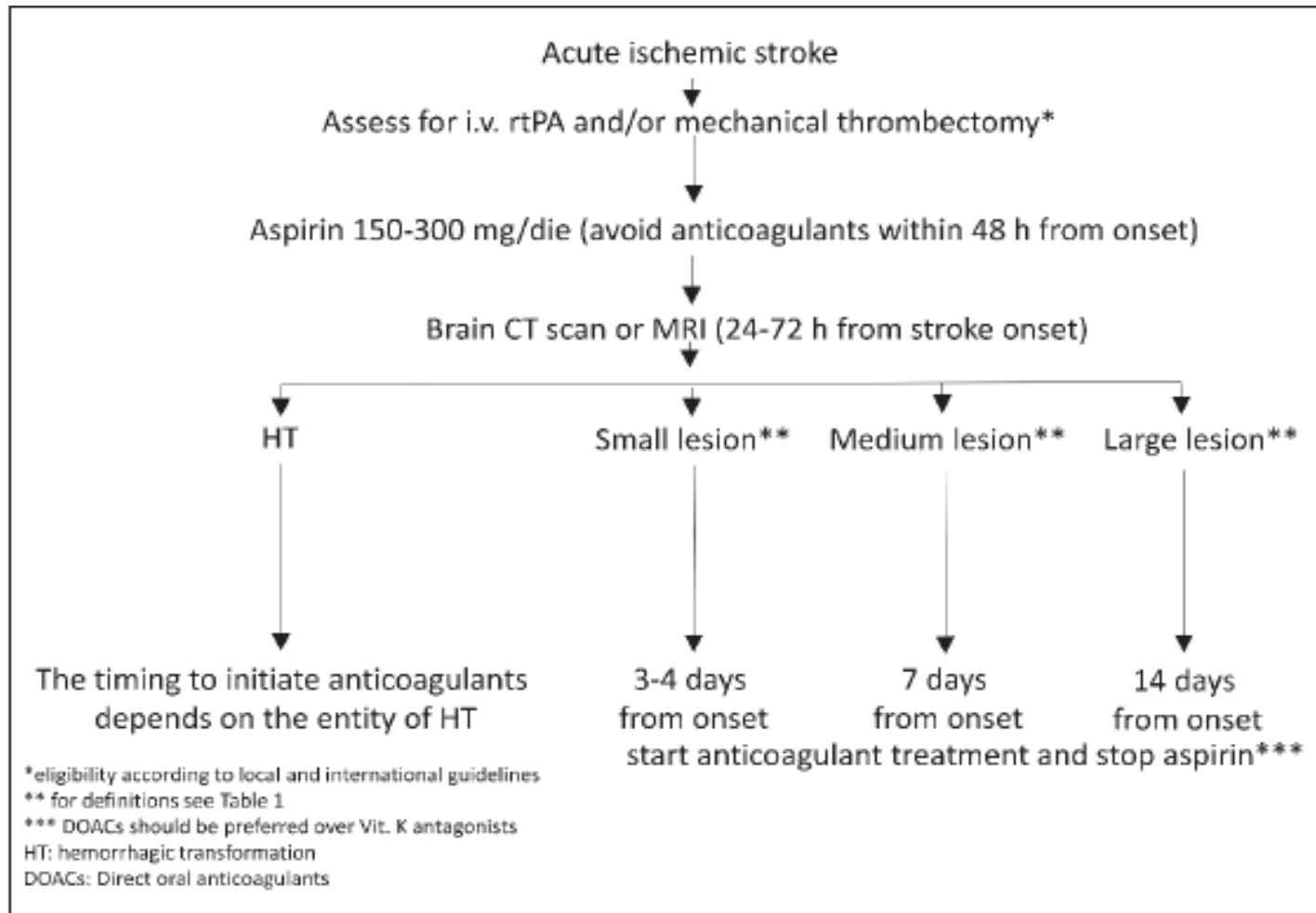


Early Recurrence and cerebral bleeding in patients with acute ischemic stroke and Atrial Fibrillation: effect of anticoagulation and its timing. The (RAF) study

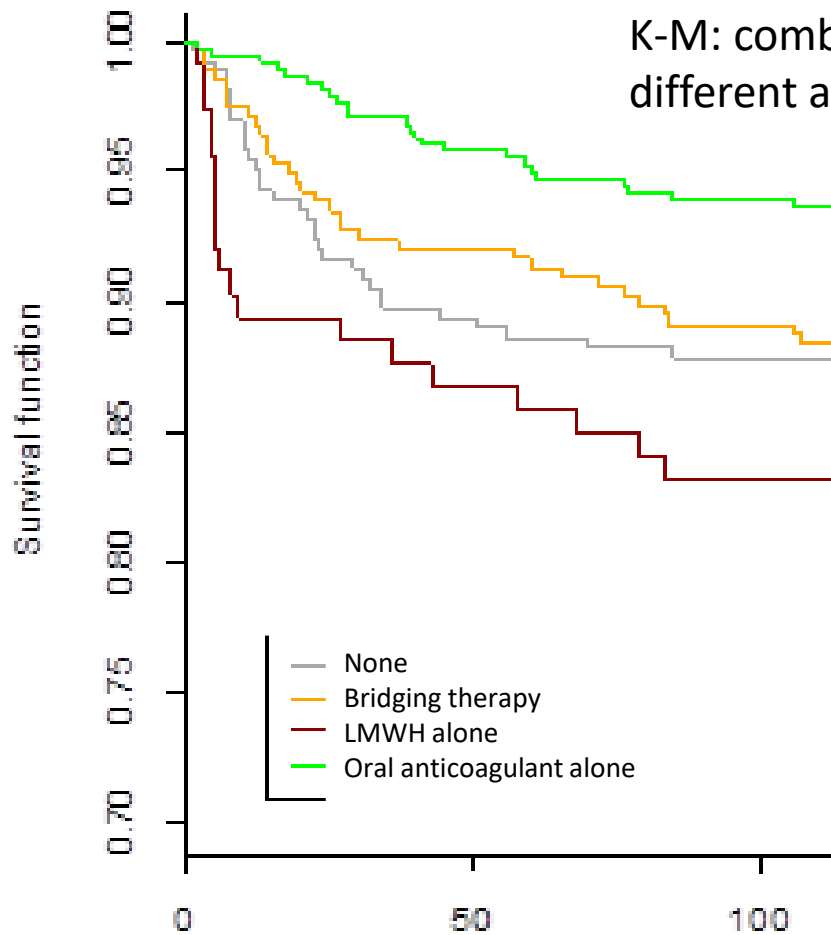
Lesion size and outcome



Timing of anticoagulation therapy in patients with acute ischaemic stroke and atrial fibrillation



K-M: combined outcome events in different anticoagulant strategies

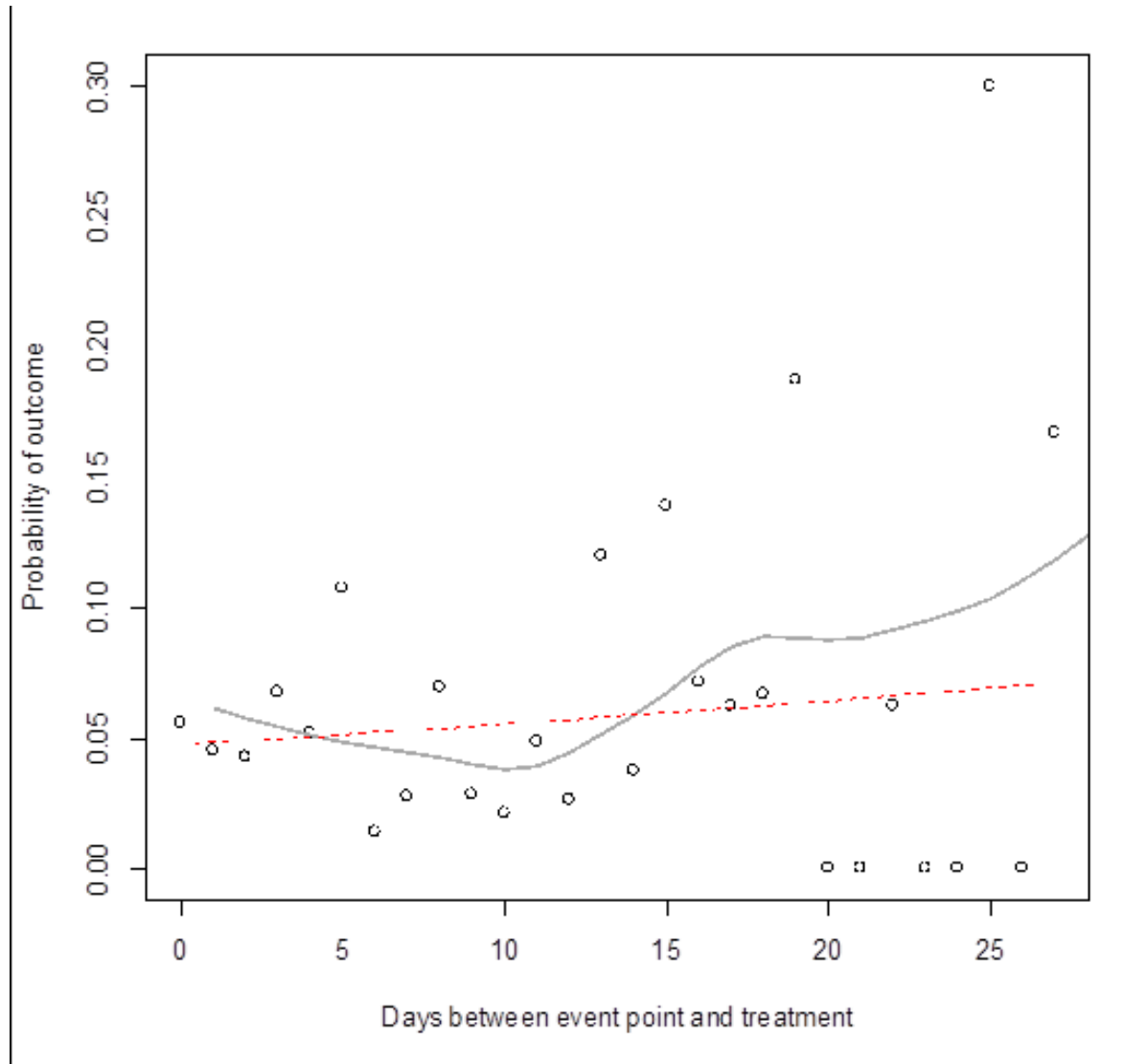


Days from index event		
263	236	232
276	254	247
113	99	95
377	362	355

Chisq= 14.2 on 3 degrees of freedom, p= 0.00262



Combined Risks of Events (ischemic and hemorrhagic) depending on the time between onset and the initiation of the DOAC therapy



Highlights

- Reperfusion therapy
- Early secondary prevention
- **Early worsening after a stroke**

Early worsening after an ischemic stroke

1-2 every 5 patients

- Causes related to arterial occlusion or cerebral infarct
- Systemic causes

At risk situations

- MCA stroke malignant MCA syndrome
- Cerebellar stroke acute hydrocephalus
- Posterior stroke basilar occlusion
- Severe (tight) carotid stenosis carotid occlusion
- Artery dissection cerebral embolization
- Lacunar stroke progression of the deficit

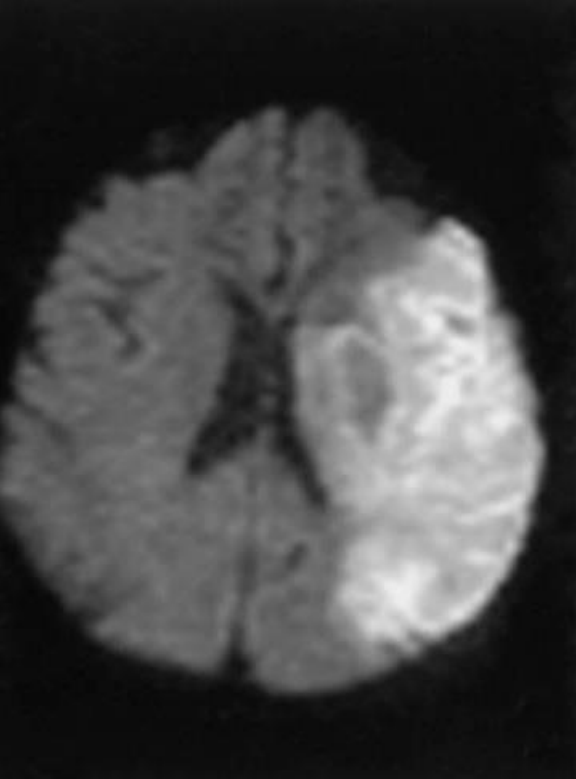
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Malignant MCA stroke

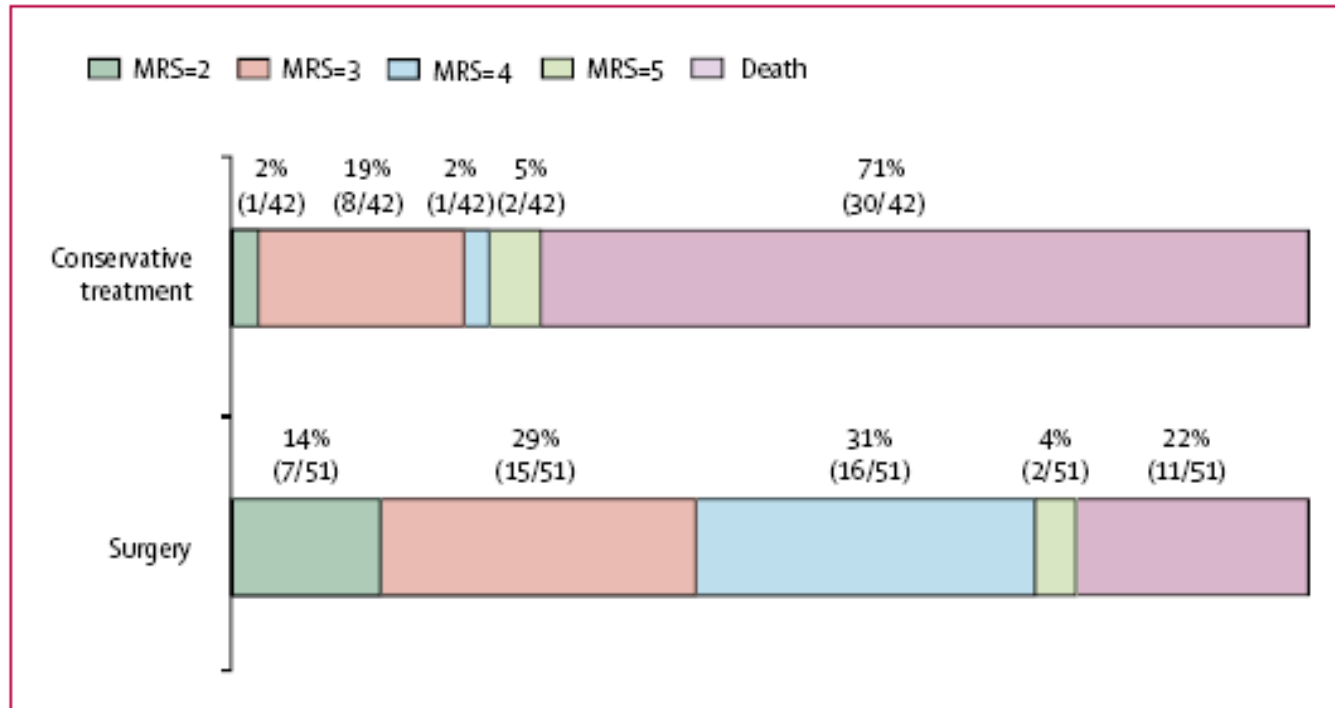
Inclusion criteria

- Age 18–60 years
- Clinical deficits suggestive of infarction in the territory of the MCA
- NIHSS >15
- Decrease in the level of consciousness to a score of 1 or greater on item 1a of the NIHSS
- Signs on CT of an infarct of at least 50% of the MCA territory or infarct volume >145 cm³ as shown on diffusion-weighted MRI
- Surgery within 48 h after onset of symptoms

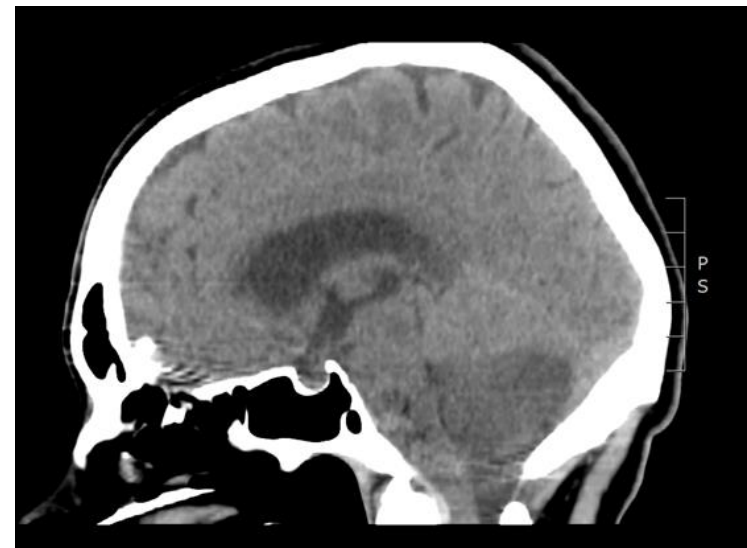
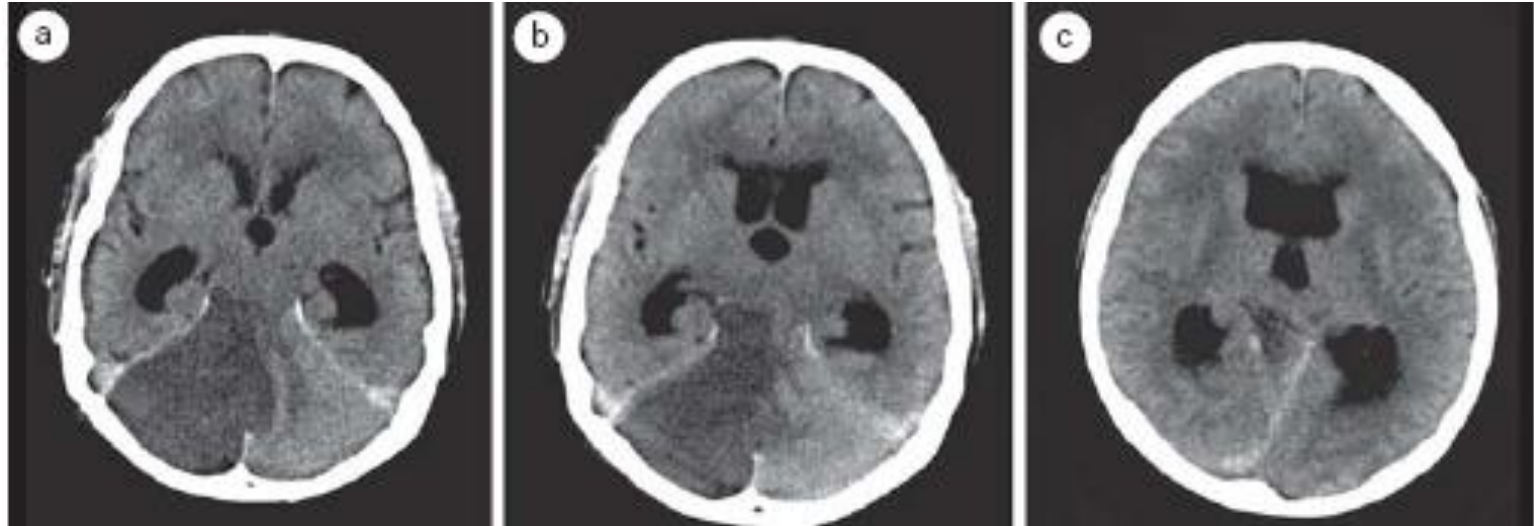
Exclusion criteria

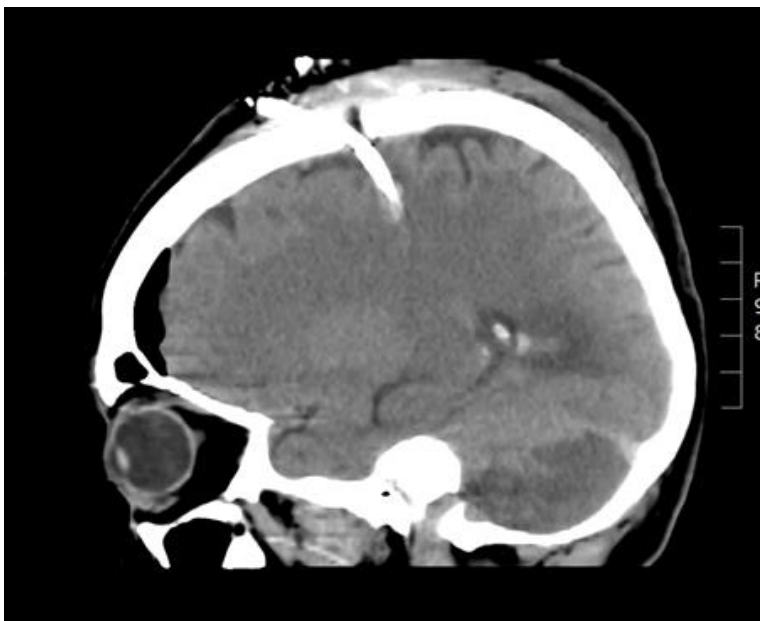
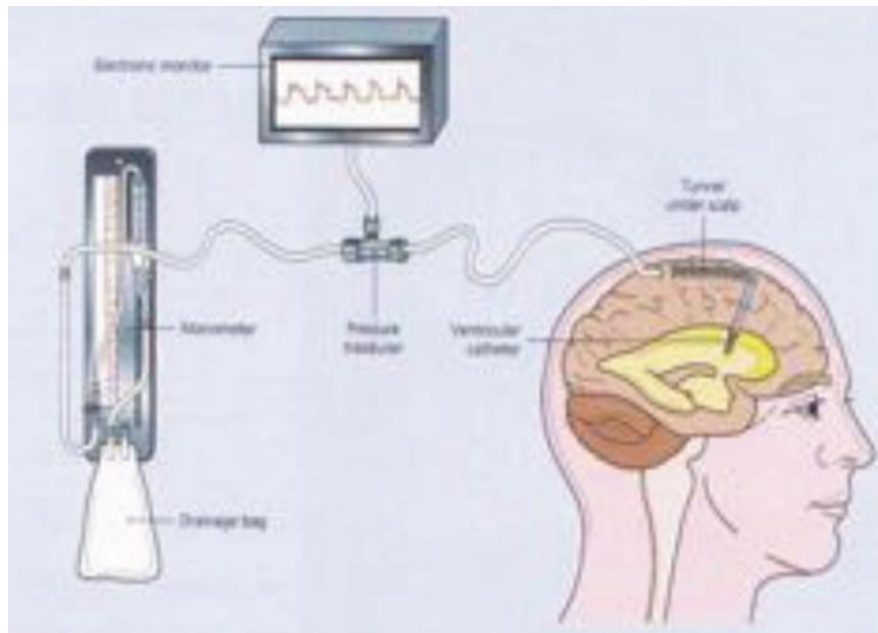
- Prestroke score on the mRS ≥ 2
- Two fixed dilated pupils
- Contralateral ischaemia or other brain lesion that could affect outcome
- Space-occupying haemorrhagic transformation of the infarct (\geq parenchymal haemorrhage grade 2)
- Life expectancy <3 years
- Other serious illness that could affect outcome
- Known coagulopathy or systemic bleeding disorder
- Contraindication for anaesthesia
- Pregnancy

Malignant MCA stroke



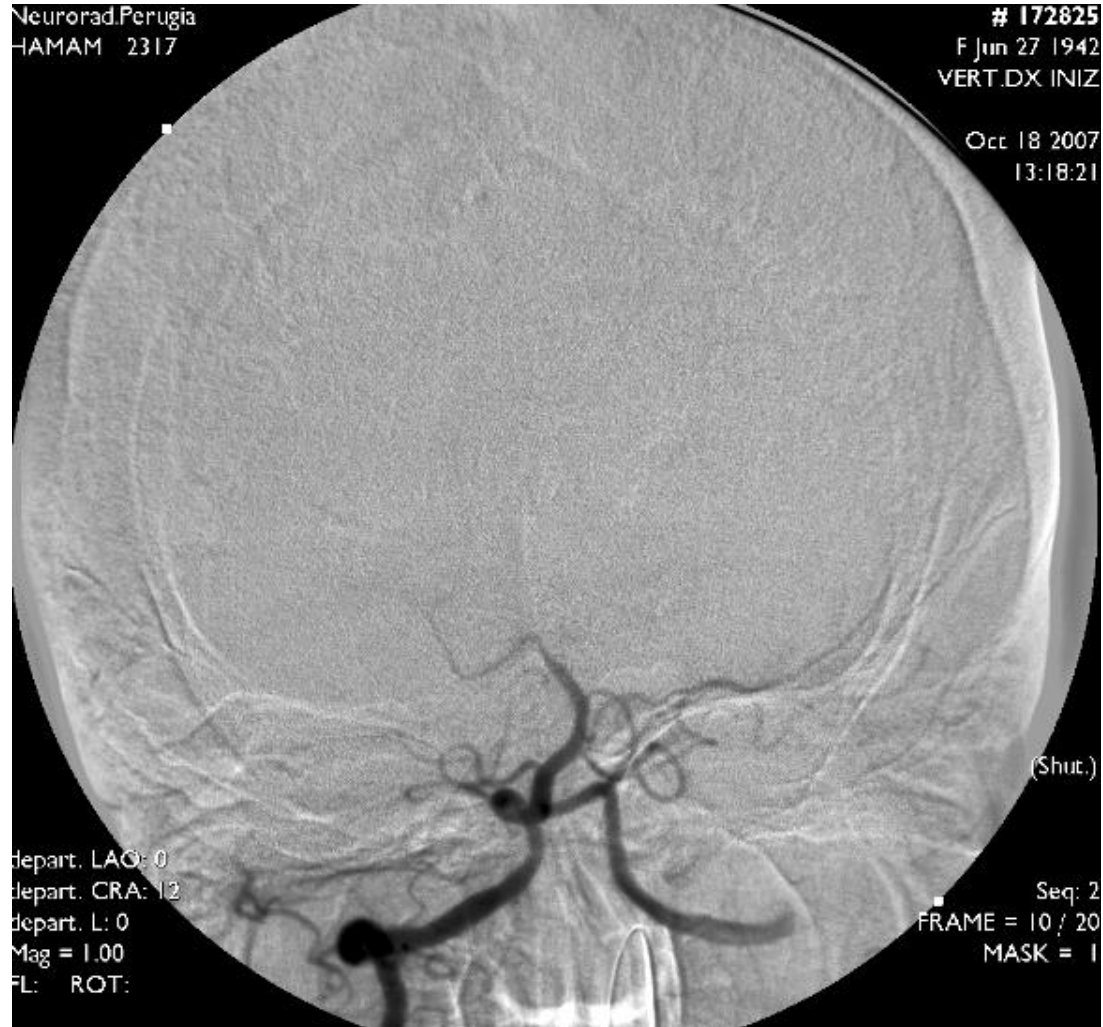
Cerebellar stroke







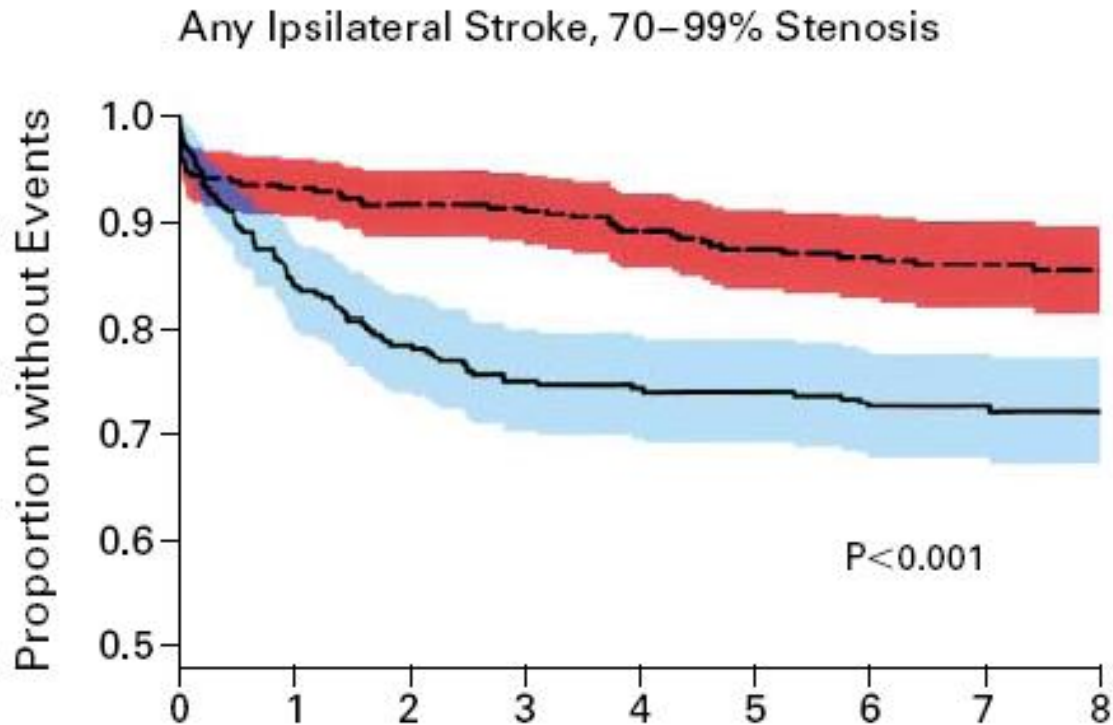
Posterior stroke: basilar occlusion



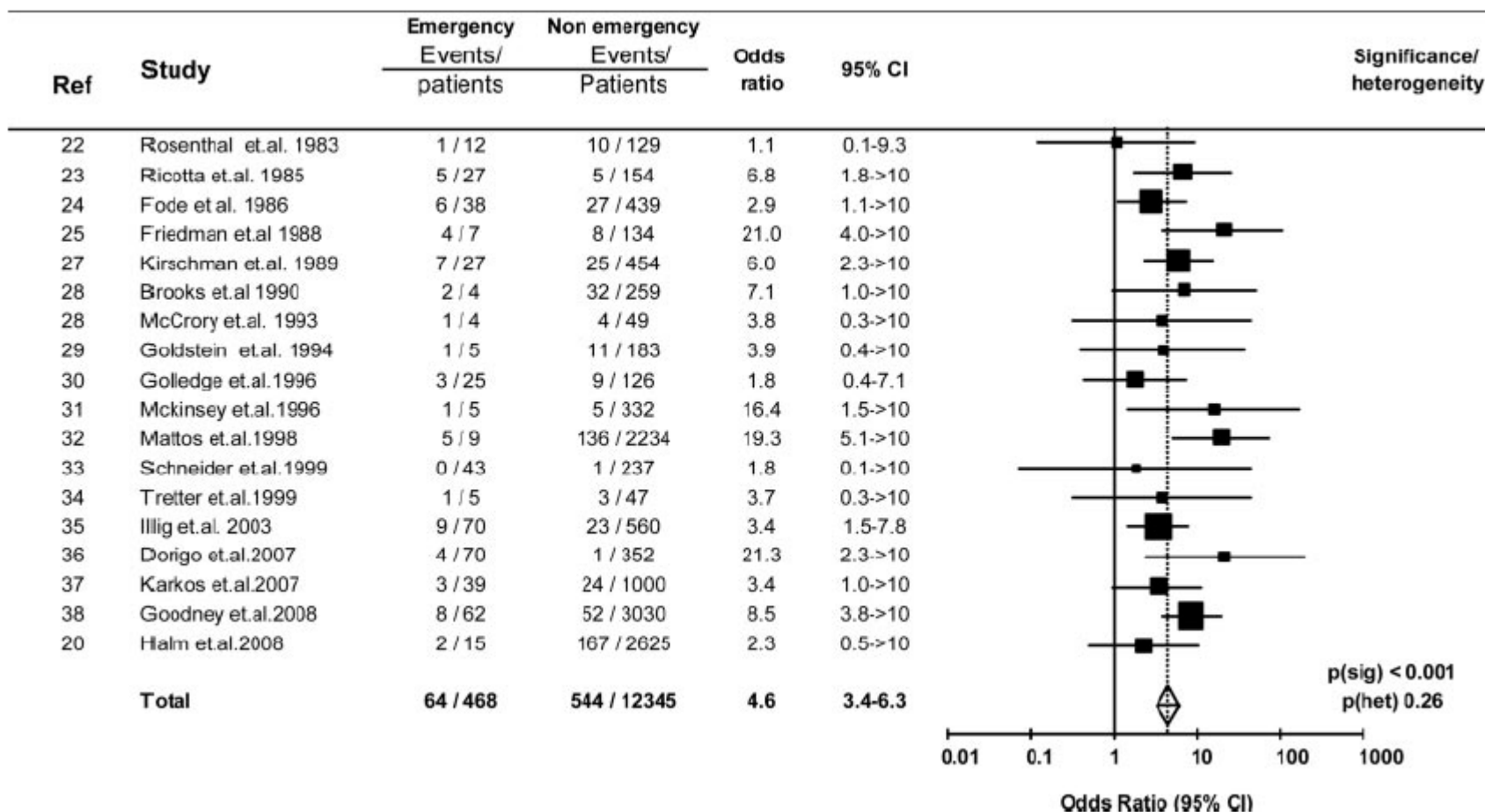
Posterior stroke: basilar occlusion



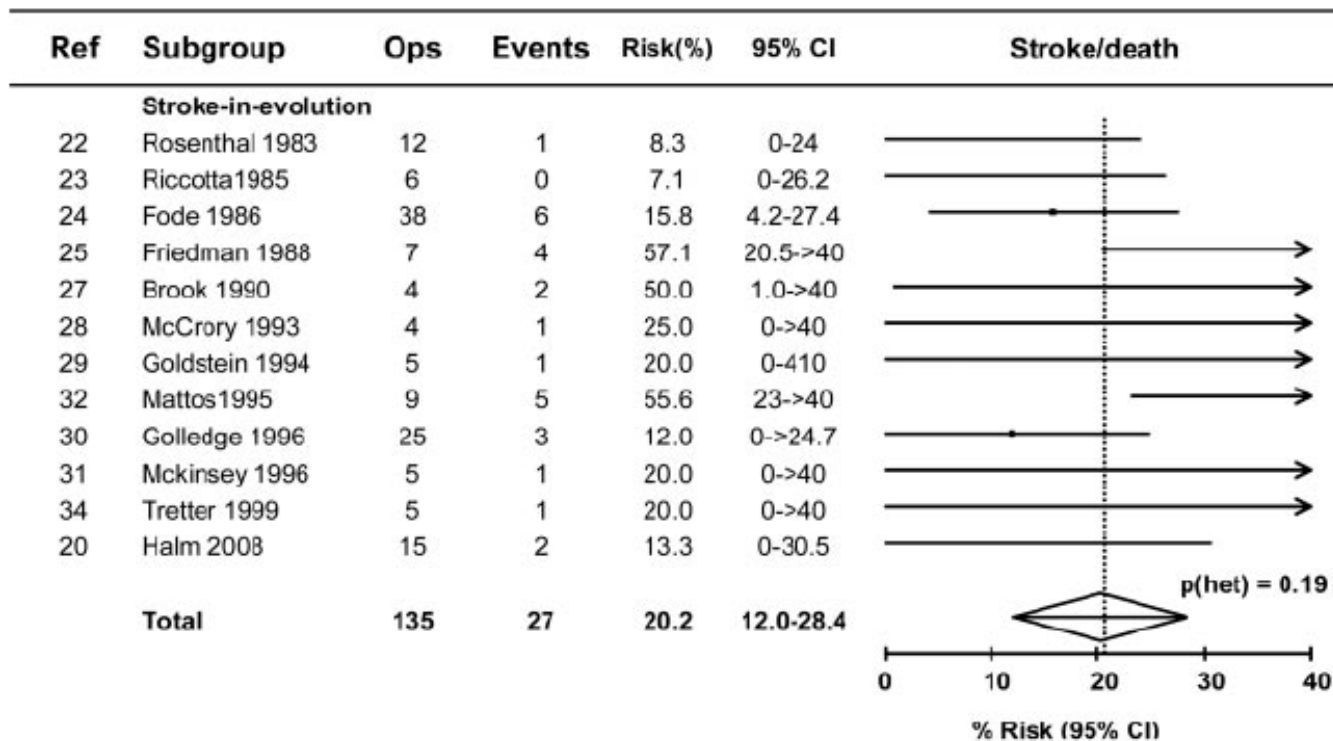
Severe (tight) carotid stenosis Benefit Of Carotid Endarterectomy In Patients With Symptomatic Severe Stenosis



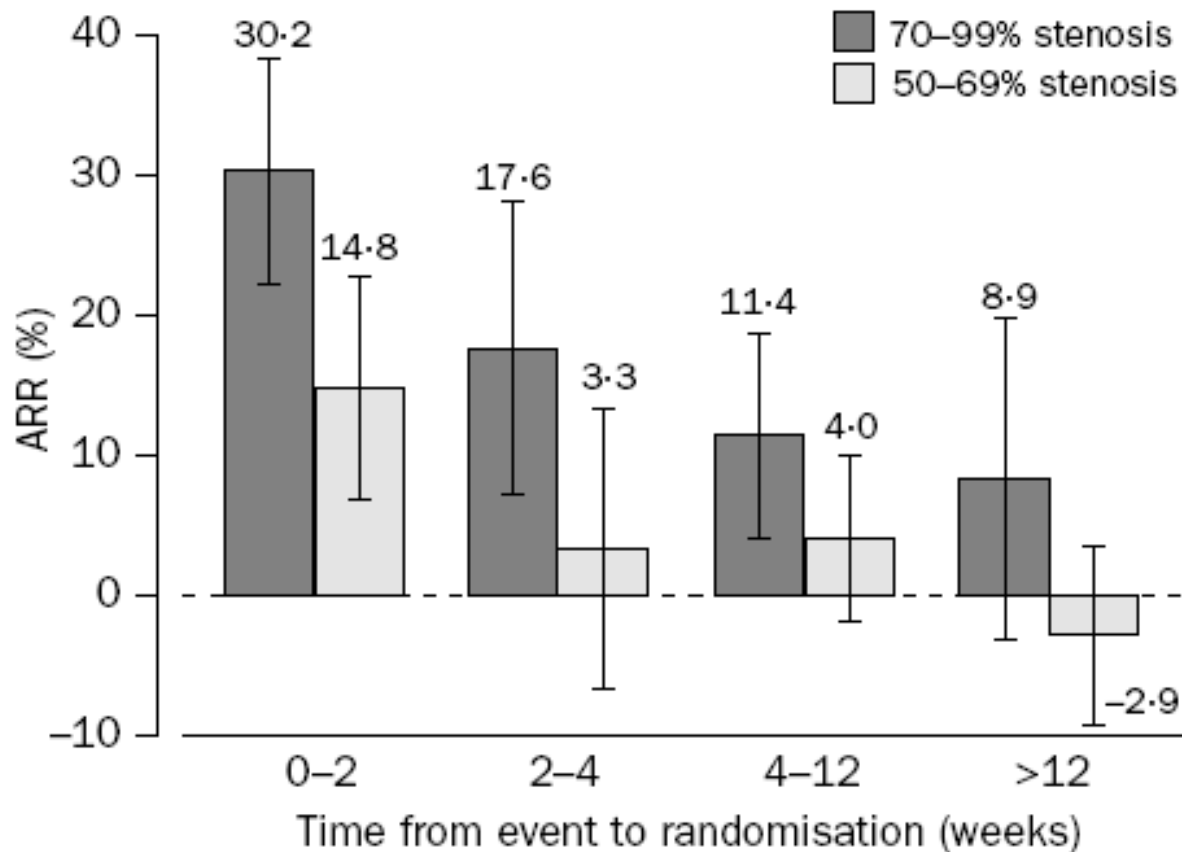
Operative stroke and death after emergency carotid endarterectomy for unstable neurological deficit (crescendo TIA and stroke in evolution) vs nonemergency surgery.



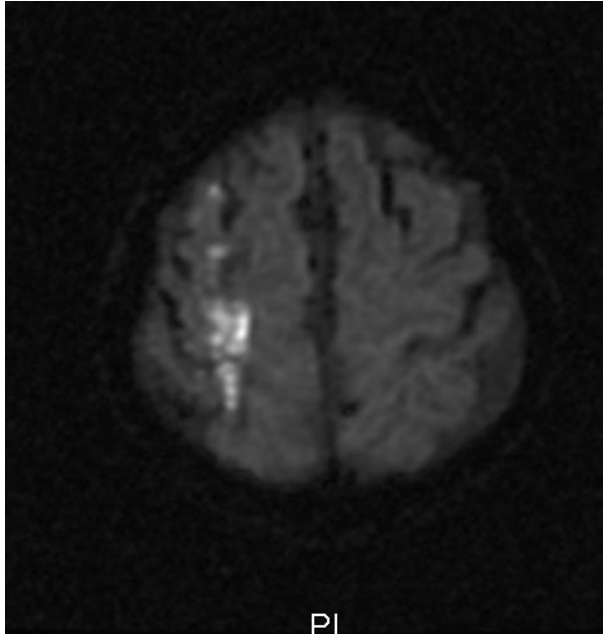
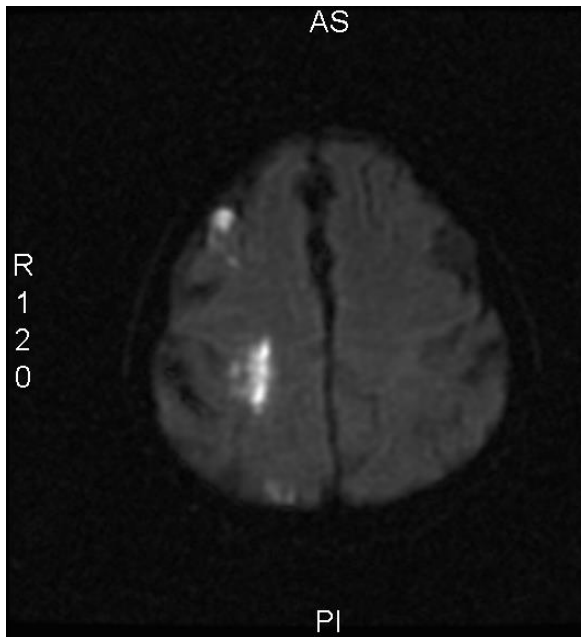
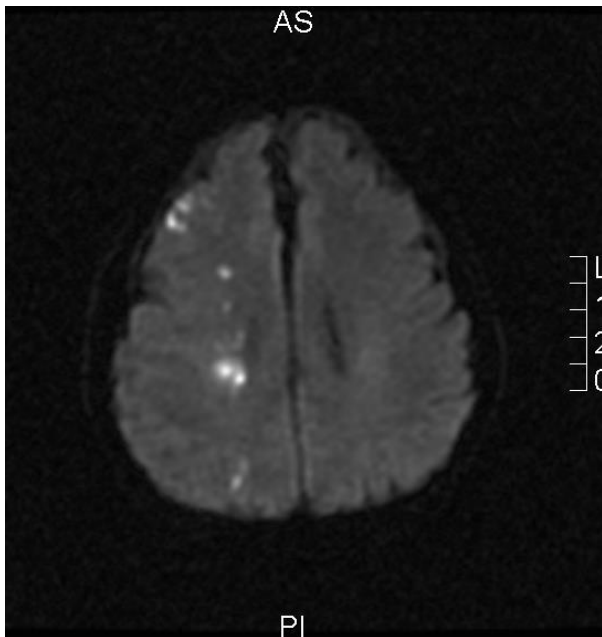
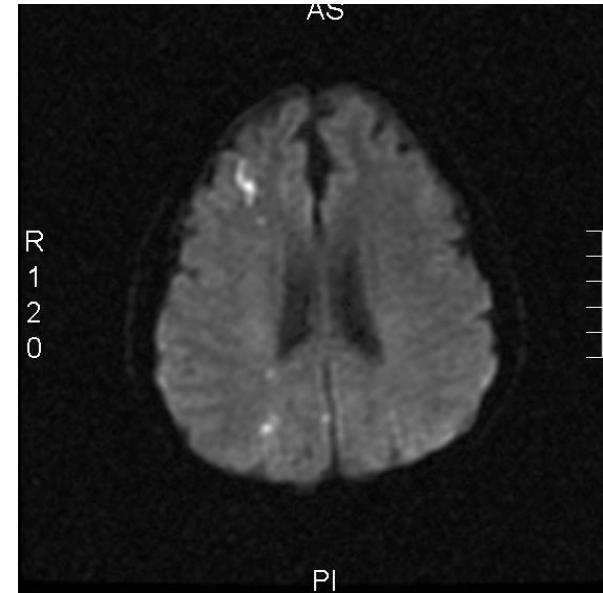
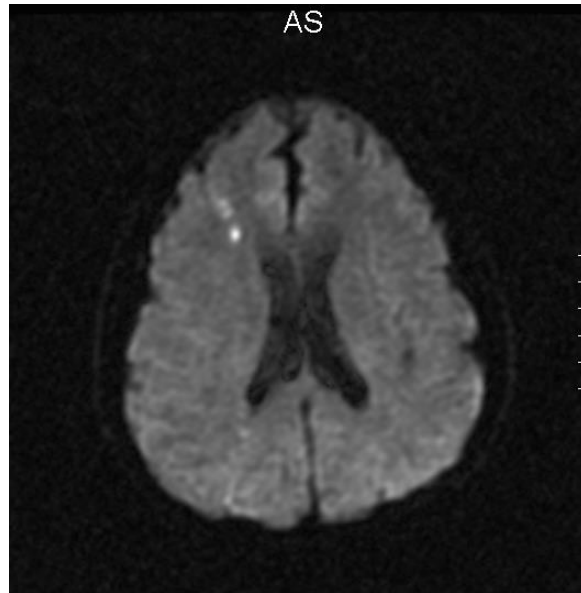
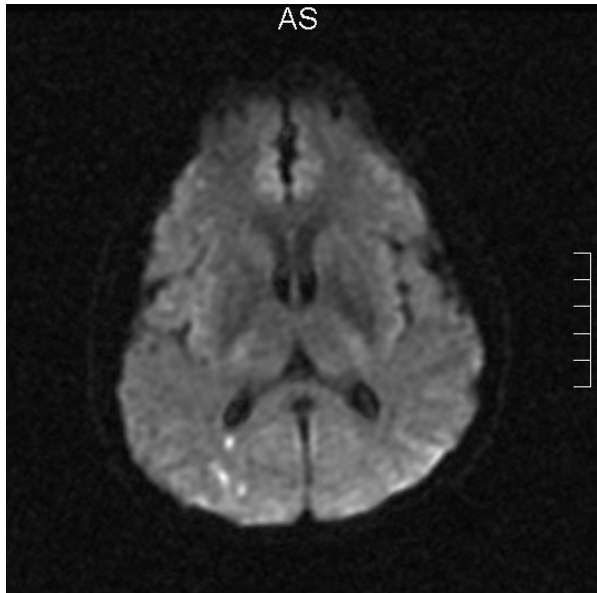
Operative stroke and death after emergency carotid endarterectomy for unstable neurological deficit (stroke in evolution) vs nonemergency surgery.



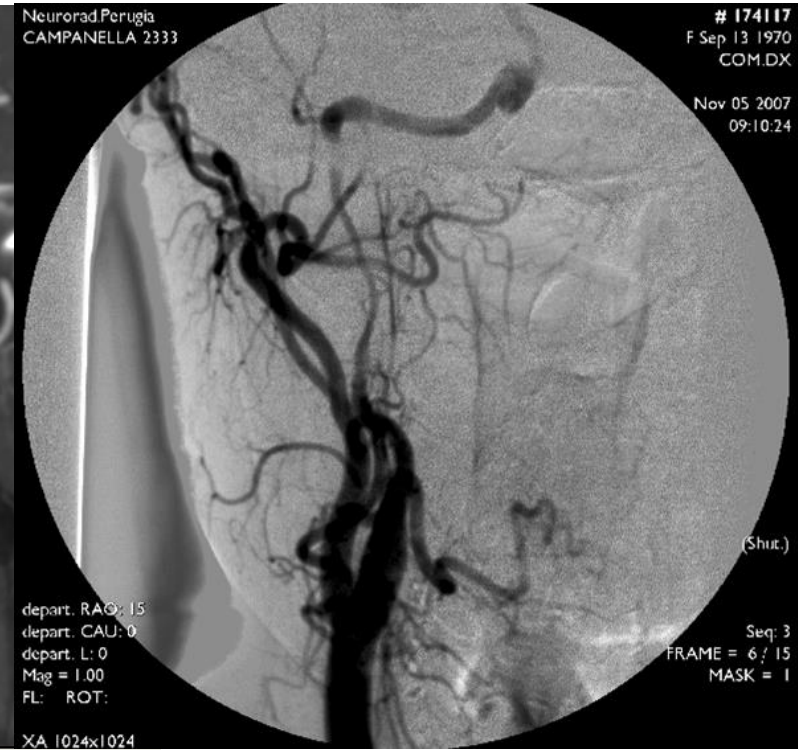
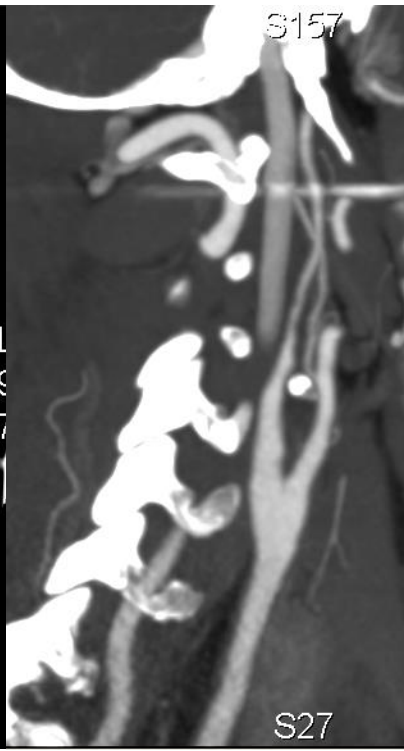
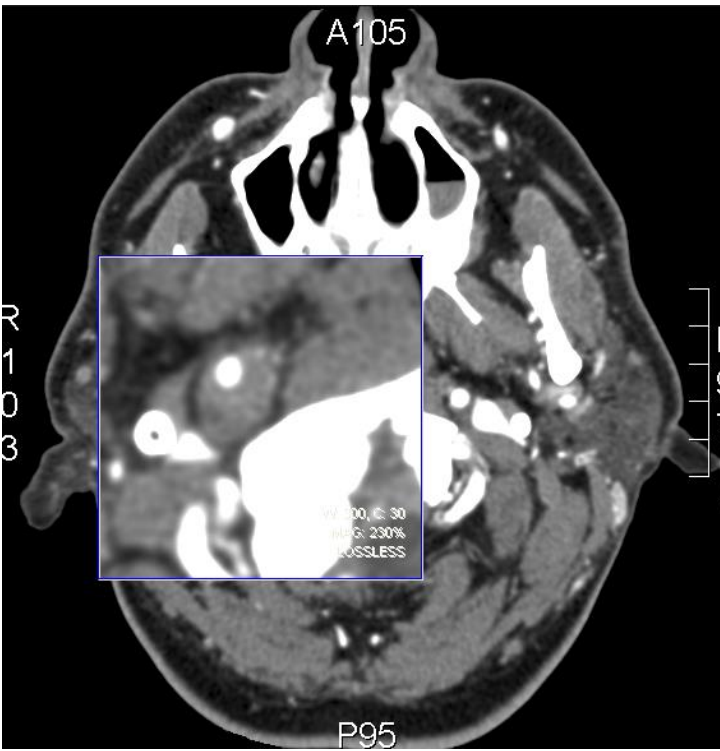
Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery



Border-zone infarct



Artery dissection



Artery dissection

Consider antithrombotic treatment

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graph TD; A[Consider antithrombotic treatment] --> B[Antiplatelet therapy  
Patient at high risk of bleeding  
Enlarging intramural hematoma  
Hemodynamic impairment  
Intacranial arterial dissection, Large stroke]; A --> C[Anticoagulation  
Progression on antiplatelet therapy  
Dissected artery occlusion  
Free floating thrombus  
Evidence of cerebral embolism];
```

Antiplatelet therapy

Patient at high risk of bleeding
Enlarging intramural hematoma
Hemodynamic impairment
Intacranial arterial dissection, Large stroke

Anticoagulation

Progression on antiplatelet therapy
Dissected artery occlusion
Free floating thrombus
Evidence of cerebral embolism

Neurorad, Perugia
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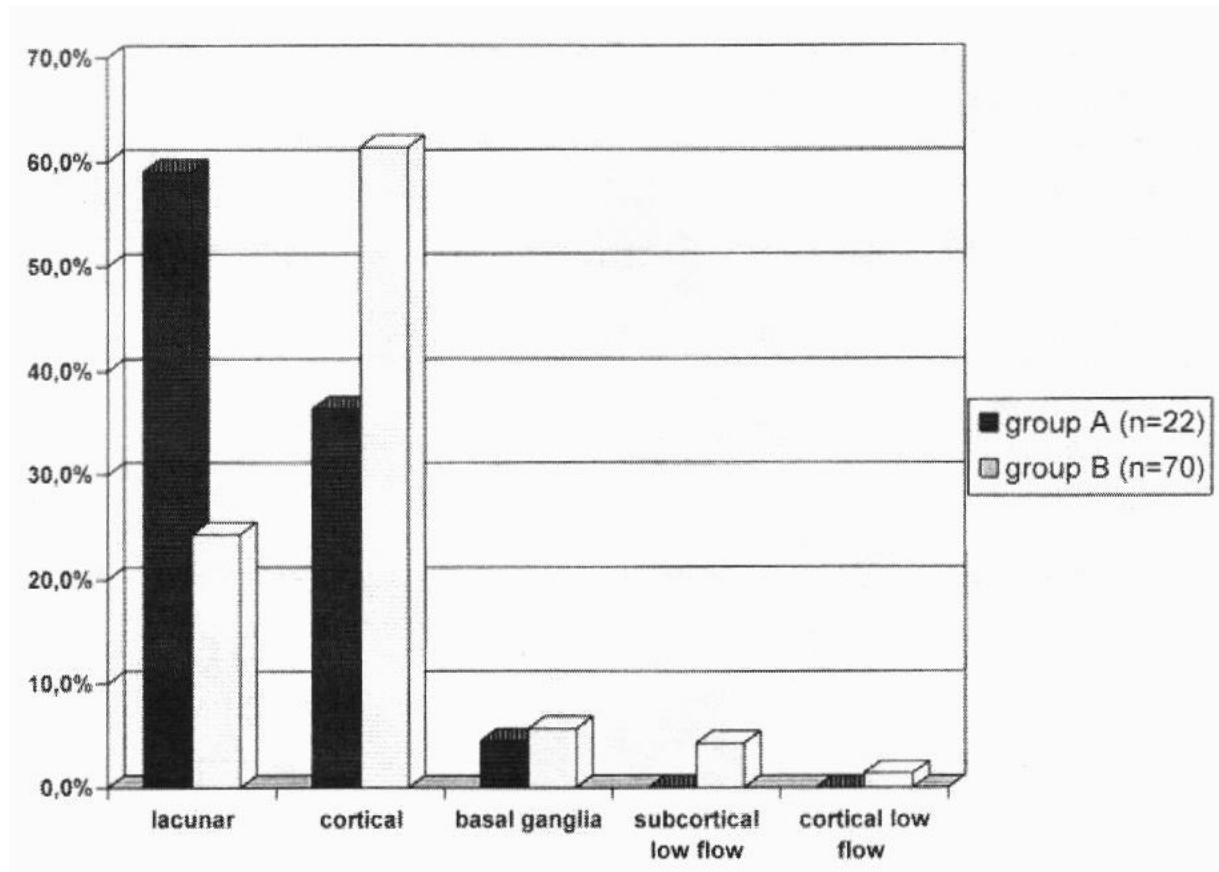
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Lacunar stroke



Group A: with progressive motor deficit

Group B: without progressive motor deficit

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THE
WALL