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Periinterventional management in acute neuro-intervention

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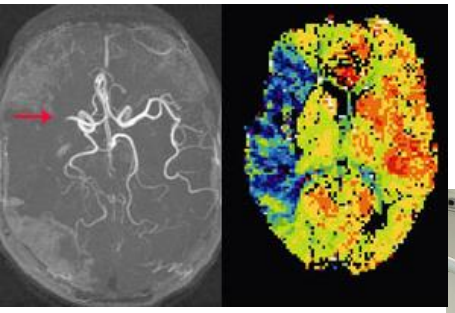

- There are 2 evidence based treatment options for acute ischemic stroke:
  Stroke unit treatment and systemic thrombolysis with rtPA [1]

- Recommended door to needle-time for i.v. thrombolysis < 60 minutes (AHA/ASA guidelines)

- Gold standard i.v. thrombolysis : < 30 minutes [2,3]

[1] Stroke Unit Trialists' Collaboration Cochrane Database Syst Rev. 2007: CD000197
[2] Meretoja A et al. Neurology. 2012; 79:306-313
[3] Ford AL et al. Stroke 2012; 43: 3395-3398

NNT of systemic intravenous lysis

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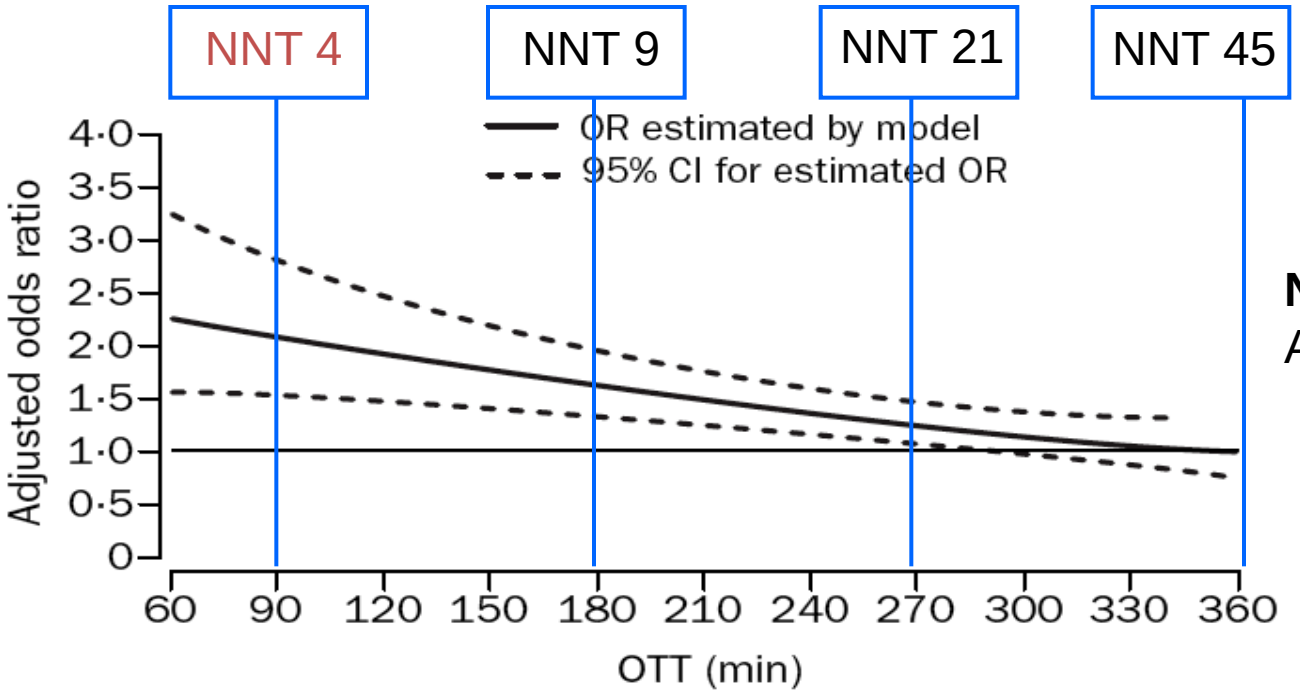
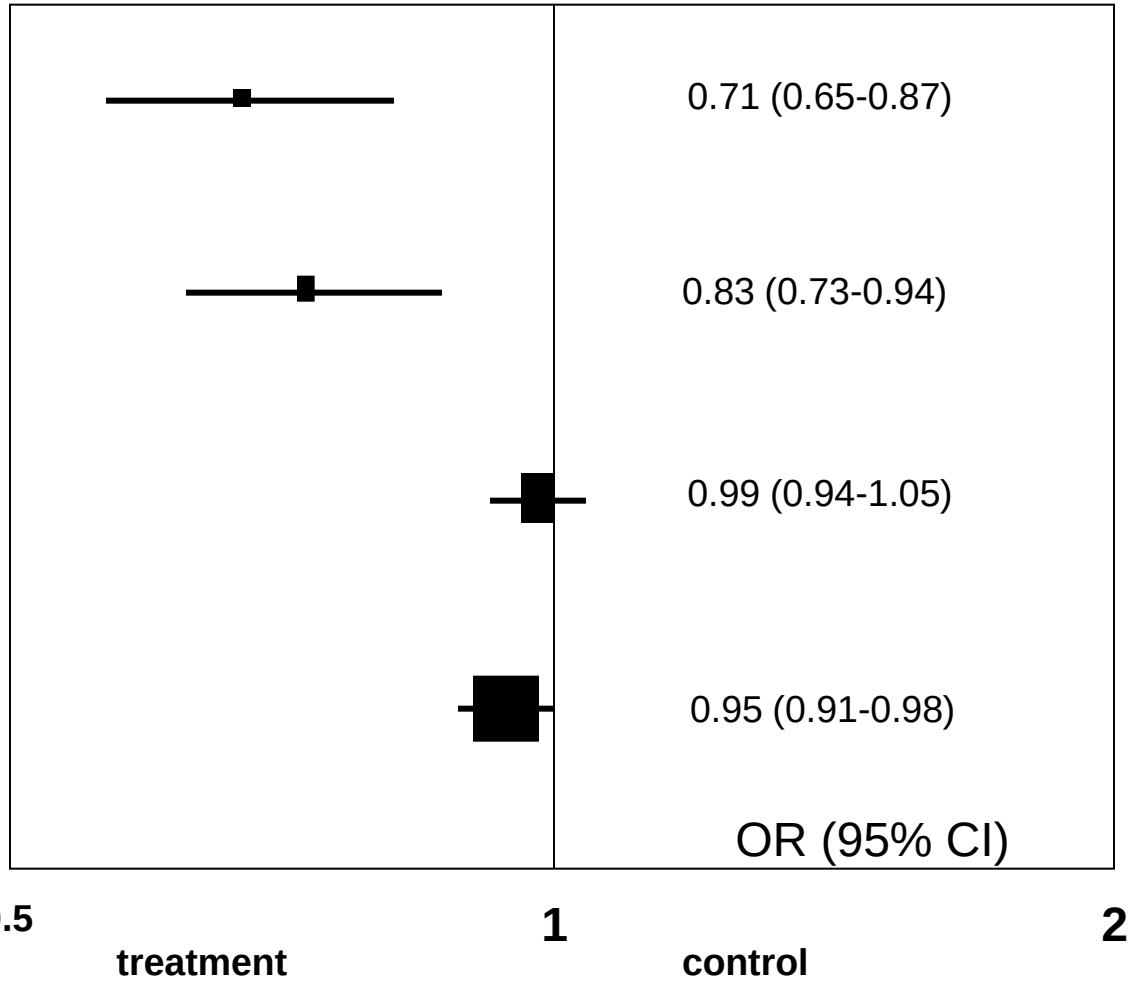


NINDS, ECASS I und II, ATLANTIS

‚Association of outcome with early stroke treatment: pooled analysis of ATLANTIS; ECASS, and NINDS rt-PA stroke trials. ' Lancet 2004



The Cochrane Collaboration 3, 2005
Candelise, Lancet 2007

The Impact of Recanalization on Ischemic Stroke Outcome

A Meta-Analysis

Joung-Ho Rha, MD; Jeffrey L. Saver, MD

Stroke 38, 967 (2007)

- 1985-2002:
- 53 studies with recanalization data (n=2066)

- outcome data: 33 studies (n=998)

	recanalization (%)
spontaneous	24,1
i.v. lysis	46,2
i.a. lysis	63,2
i.v./i.a. combined	67,5
mechanic devices	**83,6**

Update 2013

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7.2.13 The New England Journal of Medicine

3 controlled studies on interventional treatment

1. IMS-3-Study
2. SYNTHESIS
3. MR-RESCUE

All three studies „negative“ without additional benefit for the patient

Endovascular Treatment for Acute Ischemic Stroke — Still Unproven NEJM 2013

Alfried Krupp Krankenhaus

A Trial of Imaging Selection and Endovascular Treatment for Ischemic Stroke
Chelsea S. Kidwell, et al, for the MR RESCUE Investigators*N Engl J Med 2013.
DOI: 10.1056/NEJMoa1212793

Results

Among 118 eligible patients, the mean age was 65.5 years, the mean time to enrollment was 5.5 hours, and 58% had a favorable penumbral pattern. Revascularization in the embolectomy group was achieved in 67% of the patients. Ninety-day mortality was 21%, and the rate of symptomatic intracranial hemorrhage was 4%; neither rate differed across groups. Among all patients, mean scores on the modified Rankin scale did not differ between embolectomy and standard care (3.9 vs. 3.9, P=0.99). Embolectomy was not superior to standard care in patients with either a favorable penumbral pattern (mean score, 3.9 vs. 3.4; P=0.23) or a nonpenumbral pattern (mean score, 4.0 vs. 4.4; P=0.32). In the primary analysis of scores on the 90-day modified Rankin scale, there was no interaction between the pretreatment imaging pattern and treatment assignment (P=0.14).

Conclusions

A favorable penumbral pattern on neuroimaging did not identify patients who would differentially benefit from endovascular therapy for acute ischemic stroke, nor was embolectomy shown to be superior to standard care.

Endovascular Treatment for Acute Ischemic Stroke — Still Unproven NEJM 2013

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Endovascular Treatment for Acute Ischemic Stroke
Alfonso Ciccone, et al., for the SYNTHESIS Expansion Investigators*N Engl J Med 2013. DOI: 10.1056/NEJMoa1213701

Results

A total of 181 patients were assigned to receive endovascular therapy, and 181 intravenous t-PA. The median time from stroke onset to the start of treatment was 3.75 hours for endovascular therapy and 2.75 hours for intravenous t-PA (P<0.001). At 3 months, 55 patients in the endovascular-therapy group (30.4%) and 63 in the intravenous t-PA group (34.8%) were alive without disability (odds ratio adjusted for age, sex, stroke severity, and atrial fibrillation status at baseline, 0.71; 95% confidence interval, 0.44 to 1.14; P=0.16). Fatal or nonfatal symptomatic intracranial hemorrhage within 7 days occurred in 6% of the patients in each group, and there were no significant differences between groups in the rates of other serious adverse events or the case fatality rate.

Conclusions

The results of this trial in patients with acute ischemic stroke indicate that endovascular therapy is not superior to standard treatment with intravenous t-PA.

Endovascular Treatment for Acute Ischemic Stroke — Still Unproven NEJM 2013

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Endovascular Therapy after Intravenous t-PA versus t-PA Alone for Stroke
Joseph P. Broderick, et al, for the Interventional Management of Stroke (IMS) III Investigators N Engl J Med 2013. DOI: 10.1056/NEJMoa1214300

The study was stopped early because of futility after 656 participants had undergone randomization (434 patients to endovascular therapy and 222 to intravenous t-PA alone). The proportion of participants with a modified Rankin score of 2 or less at 90 days did not differ significantly according to treatment (40.8% with endovascular therapy and 38.7% with intravenous t-PA; absolute adjusted difference, 1.5 percentage points; 95% confidence interval [CI], −6.1 to 9.1, with adjustment for the National Institutes of Health Stroke Scale [NIHSS] score [8–19, indicating moderately severe stroke, or ≥20, indicating severe stroke]). Findings in the endovascular-therapy and intravenous t-PA groups were similar for mortality at 90 days (19.1% and 21.6%, respectively; P=0.52) and the proportion of patients with symptomatic intracerebral hemorrhage within 30 hours after initiation of t-PA (6.2% and 5.9%, respectively; P=0.83).

CONCLUSIONS

The trial showed similar safety outcomes and no significant difference in functional independence with endovascular therapy after intravenous t-PA, as compared with intravenous t-PA alone

Problems of IMS-III

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- 22 centers with < 5 patients, 15 centers w/o patients
- recruitment 6 years
- vessel occlusion not necessary
- experience of interventionalists low
- 334/434 „endovascular patients“ were really treated (77%)
- in 80 (24%) „untreatable thrombus“
- devices not up to date
- very low revascularisation rates
- time until angiography: 208 $\pm$ 47 Min

Open vessel, bad outcome - why?

- wrong selection?
- to late?
- to long?
- bad interventional care?
- to strong/weak anticoagulation?

Reperfusion damage

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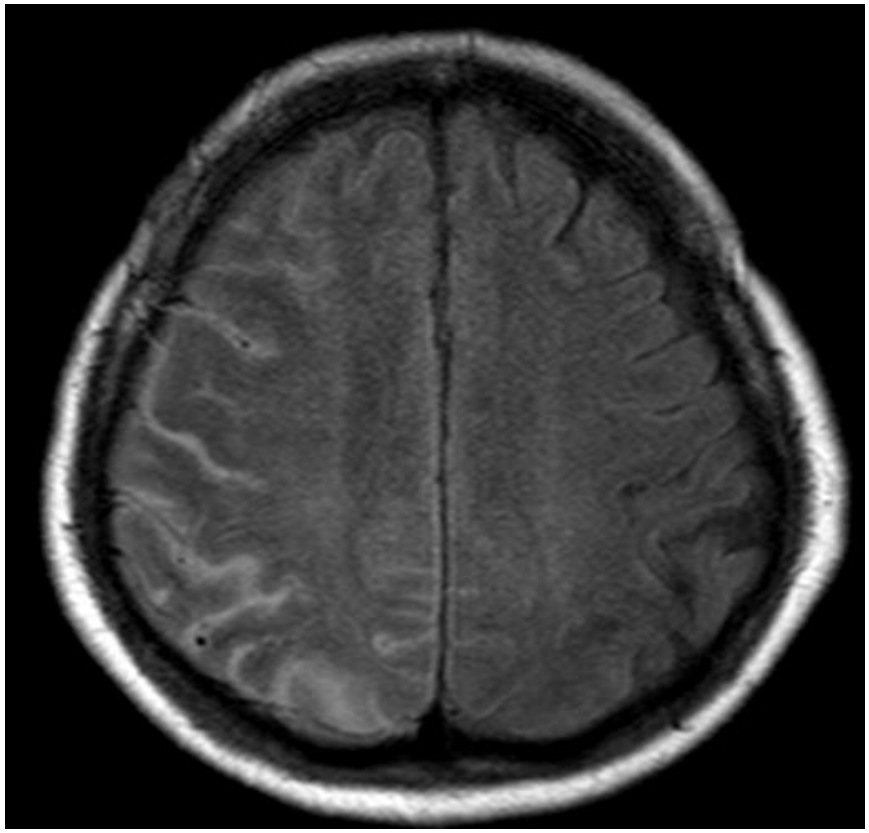

Optimal management starts before and in the emergency room

- Prehospital information of the stroke unit team by emergency personnel
- CCT with CTA
  -in wake-up strokes MRI mismatch and MRA
- Special lysis lab with PTT and INR point-of-care [1]
- „Crush intubation“

[1]Rizos et al. Stroke 2009;40:3547-51

intervention - SOP acute stroke

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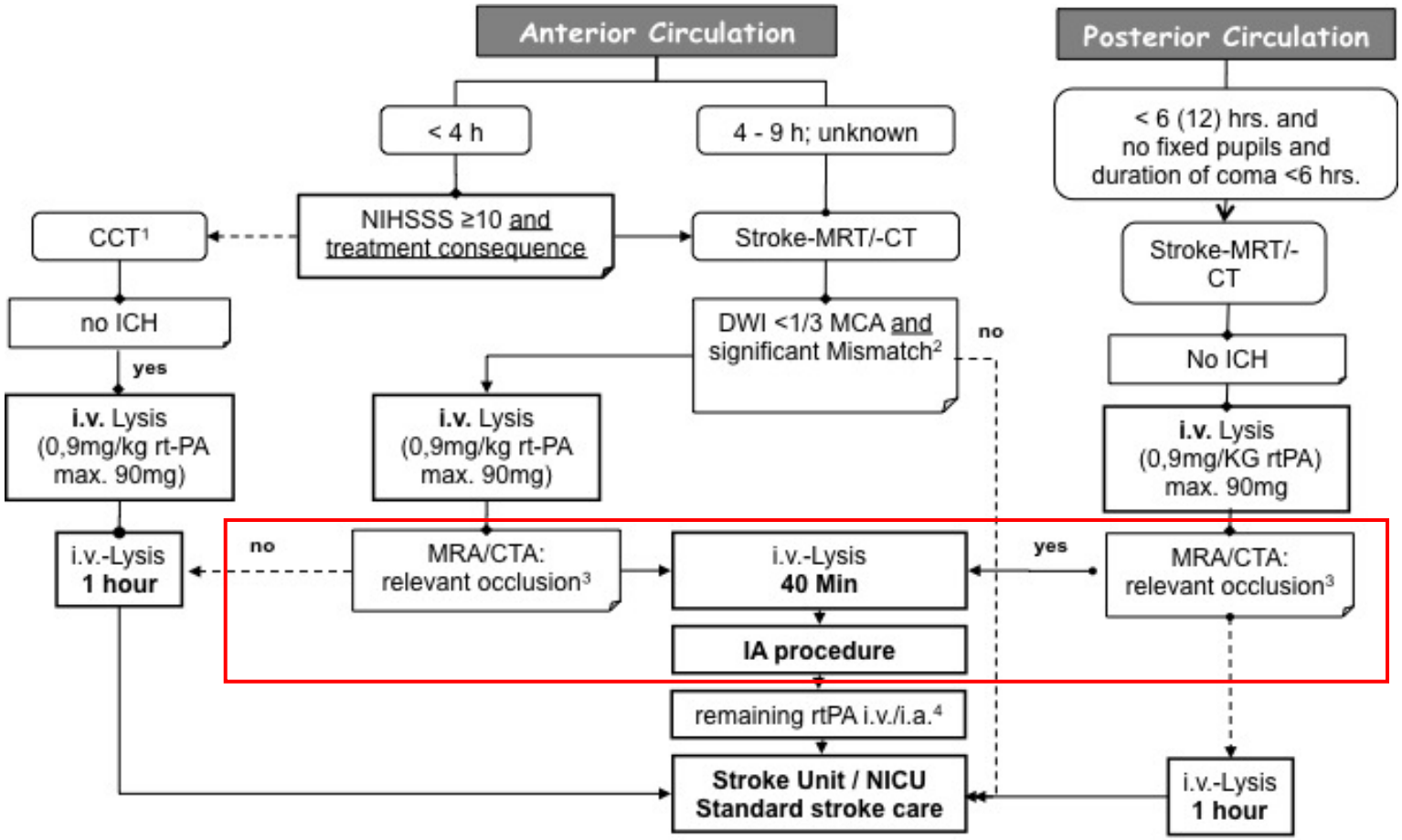

remarks:

1: before any intervention including CT-Angiography
2: MR-Mismatch: TTP-delay >6Sek
3: ICA, M1, multiple M2s, A. basilaris , dominant V4
4: if incomplete recanalization

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Indication for thrombectomy in the neurovascular network Ruhr

- Occlusion of ICA, carotid T, M1 (M2), or basilar artery

  and

- start of intervention within 6 h after first symptom

  or

- MRI mismatch in „wake-up-stroke“

  or

- fluctuating symptoms in basilar artery occlusion: no defined time window
  (contraindication: coma > 2 h)

Eyding et al. Akt. Neurol 2012, 39: 404–411

To bridge or not to bridge?

To bridge or not to bridge?

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- **pro:** - evidence based treatment until the intervention begins
- **contra:** - higher bleeding risk?
  - fragmentation of thrombi with embolisation into distal branches?
- Dosing? Standard? 2/3? 1/2? No bolus?
- another CCT/CTA after bridging before intervention?

To bride or not to bridge?

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Our strategy:

- INTERNAL patients: no i.v.-bridging before thrombectomy
- EXTERNAL patients: Standard i.v.-thrombolysis (0,9 mg/kg 10% bolus, perfusor for 1h) in the external hospital
  and
  CCT control before thrombectomy

during intervention - standards

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- Monitoring: ECG, BP, $SatO_2$, CNAP, NIRS
- Prophylactic Cristalloids
- Early Norepinephrine i.v.
- Target systolic BP: 140-160 mmHg
- Target $etCO_2$: 40-45 mmHg
- Target $SatO_2$: > 95%

during intervention - adjunctive anticoagulation?

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- Why ? → reocclusion rate 18%
- What? → e.g. Heparin 2000-3000 U, 450 U/h, ACT 150-300s
- What else? Gp IIb/IIIa - antagonists: very controversial

- Our approach: primarily, nothing additionally!
  - If stent, double platelet inhibition (Aspirin, Clopidogrel)
  - If dissection/endothelial damage at times individual postprocedural heparin or tirofiban

Janjua AJNR 2008, Nahab JSCD 2011, Lazzaro Neurology 2012

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Open questions

→ Where? Stroke unit or ICU?

→ When to extubate? as soon as possible, after CT, after 24h?

→ What temperature? Normo/hypothermia?

Recommendations:

- Reduce sedation and extubate as soon as possible
- Re-warm patient slowly according to clinical status and hemodynamics
- If problems, early CT, else CT 12h after procedure
- Early transferral to stroke unit

- With proven cardiogenic stroke (atrial fibrillation!) no anticoagulation with heparins within the first 48 hours (increased risk of bleeding!) [1]

- INSULININFARCT study: i.v.-Insulins not superior to s.c. [2]

- QASC study: protocol for temperature management (> 37,5° → paracetamol)[3]

[1] Paciaroni M et al. Stroke 2007;38: 423–430
[2] Rosso C et al. Stroke 2012; 43: 2342-2349
[3] Middleton S et al. Lancet 2011; 378:1699-1706

summary

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Prior to ...

- Fixed procedures/protocols/equipmement save time

During...

- Best periprocedural management unknown
- Target values for ventilation/stabilize hemodynamics
- Adjunctive anticoagulation unkown

After...

- Individual postprocedural management
- Avoid prolonged ventilation and ICU-stay
- Fixed procedures/protocols improve outcome

Open vessel, bad outcome - why?

- Selection is important but criteria are unclear
- Time window the same as for lysis?
- Role of collateral supply?
- Is bridging dangerous?

We need a controlled study under optimal standardized conditions!

Merci