Update on Acute Stroke Intervention

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Disclosures

- No disclosures related to this talk

Objectives

- To review the latest scientific literature on the role of endovascular intervention in patients presenting with acute ischemic stroke
Introduction/Background

Ischemic stroke is a devastating condition with high mortality and disability worldwide.

IV tPA the only proven effective therapy for acute ischemic stroke. Time window 3 hrs (NINDS trial) extended to 4.5 hrs (ECASS III) in 2008.

Limitations: narrow time window, several contraindications, and very low efficacy with large vessel occlusion (LVO; 60-80% patients with LVO die or are disabled within 90 days despite treatment with IV tPA).

Intra-arterial/endovascular treatment in selected patients shown to improve recanalization.

Three large trials published in NEJM in 2013 failed to show clinical benefit (no safety concerns): IMS III, Synthesis, MR RESCUE.

Criticism of the three trials: absence of large vessel occlusion in a large proportion, use of second-generation devices.

Conversely, four recent trials published in NEJM since December 2014 show endovascular treatment by performing mechanical thrombectomy to be safe and effective.
Basic Concepts

- Cerebrovascular anatomy:
  - Anterior vs posterior circulation
  - Large vessel occlusion (LVO)

- Time window: time of onset vs. time from last known normal

- Endovascular treatment
  - Chemical dissolution using thrombolytic such as tPA
  - Mechanical thrombectomy
    - First generation device: Merci retriever (2004)
    - Second-generation device: Penumbra aspiration (2008)
    - Third generation device: Stent retrievers 2012 (Solitaire, Trevo)
    - ADAPT technique (forced aspiration) (2014)
    - Combination of stent retriever AND forced aspiration

MR CLEAN

- MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic stroke in the Netherlands)

- A Randomized Trial of Intra-arterial Treatment for Acute Ischemic Stroke; Dec 2014, NEJM

- Objective: Compare standard treatment with standard treatment PLUS endovascular treatment for patients with anterior circulation ischemic strokes secondary to large vessel occlusion who could be treated within six hours
MR CLEAN: Methods

- 16 centers in Netherlands
- Total 500 patients, mean age 65 years (23-96 years)
- 89% received IV tPA prior to randomization
- 233 randomized to endovascular treatment, 267 to standard treatment
- Retrievable stents used in most patients
- Median time from stroke onset to IV tPA: 85 minutes
- Median time from stroke onset to groin puncture: 260 minutes

MR CLEAN: RESULTS

- Primary outcome: favorable outcome of mRS 2 or less at 90 days
  - 32.6% for intervention group vs. 19.1% for standard care group
    (absolute difference of 13.5%; odds ratio 1.67; CI 1.21-2.3)
- Secondary outcomes (NIHSS at 24 hrs, NIHSS at 5-7 days, NIHSS discharge, Barthel index at 90 days) all favored intervention
- Imaging outcome: final infarct volume: 49 cc vs 79 cc
- Safety outcomes: no significant differences in mortality (~18% at 30 days for both) or rate of symptomatic ICH (~7% for both)

MR CLEAN

- Conclusion: Endovascular treatment in patients with anterior circulation acute ischemic stroke caused by LVO and initiated within 6 hrs from symptoms onset is effective AND safe
MR CLEAN: Main Points
- Six hours time window for intervention initiation
- No wait to see if patient gets better with IV tPA
- Use of stent retriever device
- No increased risk of mortality of sICH compared to IV tPA alone

ESCAPE
- ESCAPE (Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times)
- Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke; NEJM February 2015
- Objective: To evaluate endovascular treatment in addition to standard treatment in patients with acute ischemic stroke with a proximal intracranial arterial occlusion, small infarct core, and moderate to good collateral circulation

ESCAPE Methods
- Multicenter, prospective, randomized, open-label, controlled, with blinded outcome
- Patients randomized to standard care vs. stand care PLUS mechanical Thrombectomy (1:1)
- No upper age limit
- Time window 12 hours from symptoms onset or last known normal
ESCAPE Methods

- CT and CTA on all patients
- Assessed infarct core volume and collaterals
- Patients with large infarct core or poor collaterals were excluded
- Target CT to groin puncture 60 minutes
- Target CT to first reperfusion 90 minutes
- Endovascular treatment: Recommended stent retrieval PLUS forced aspiration; balloon guide catheter

ESCAPE Results

- Trial stopped early, unplanned interim analysis following publication of MR CLEAN
- 22 centers worldwide (11 Canada, 6 USA, 3 S. Korea, 1 UK, 1 Ireland)
- 316 participants: 165 in intervention group and 150 in control group; 1 excluded
- Total 238 (75%) received IV tPA

Primary outcome: mRS at 90 days for intervention plus standard care vs. standard care alone 53% vs. 29.3%

- Mortality 10.4 vs. 19% (p 0.04)
- sICH 3.6% vs. 2.7% (p 0.75)
- Barthel Index of 95-100 at day 90: 57.7% in intervention group vs. 32.6% in control

Total 49 patients (15.5%) underwent randomization after 6 hrs; study not powered enough to assess results in this subgroup
ESCAPE

- Differences from MR CLEAN
  - Time window up to 12 hours; but again powered enough only for up to 6 hrs
  - Use of imaging to exclude participants
  - More robust results in terms of good outcome (93% vs. 32.6%) and also reduced mortality
  - Even less rate of sICH (3.6% vs. 7%)
  - Better recanalization rate (72% vs. 60%)

- Similarities to MR CLEAN
  - No upper age limit for treatment
  - No wait to see if patient gets better with IV tPA

EXTEND IA

- EXTEND-IA (Extending the Time for Thrombolysis in Emergency Neurological Deficits – Intra-Arterial)

- Endovascular Therapy for Ischemic Stroke with Perfusion Imaging Selection; NEJM February 2015

- Objective: To test whether more advanced imaging selection, recently developed devices, and earlier intervention improve outcomes with endovascular therapy

EXTEND-IA Methods

- 100 planned patients in Australia and New Zealand
- Patients randomized to IV tPA alone vs. IV tPA PLUS mechanical Thrombectomy with Solitaire stent retriever

- Imaging modality: CT/CTA/CTP

- Ischemic core of less than 70 ml and salvageable brain tissue on CTP
- Mechanical thrombectomy performed within 6 hrs
EXTEND-IA Methods

- **Primary outcomes:**
  - Reperfusion at 24 hours
  - Early neurological improvement at day 3 (equal to or greater than 8 point reduction on NIHSS or score of 0 or 1)

- **Secondary outcome:** mRS at 90 days

EXTEND-IA Results

- Trial stopped early after MR CLEAN
- Interim analysis performed with total 70 patients only (35 each group)
  - Median stroke onset to groin puncture: 210 minutes
  - Median hospital arrival to groin puncture: 113 minutes
  - Median hospital arrival to reperfusion: 156 minutes
  - Recanalization rate: 86%
EXTEND-IA

Main points:
- Use of imaging to exclude participants improved outcome
- More robust results (good clinical outcome 70% vs. 53% vs. 32.6%)
- No upper age limit
- No wait to see if patient gets better with IV tPA
- No significant increased risk of mortality of sICH compared to IV tPA alone

SWIFT-PRIME

SWIFT-PRIME (Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment)

Stent-Retriever Thrombectomy after Intravenous tPA vs. tPA Alone in Stroke; NEJM April 2015

Objective: To test if thrombectomy with a stent retriever, in addition to IV tPA, increases reperfusion rate and improve long-term functional outcome

SWIFT-PRIME Methods

Imaging: Proximal large vessel occlusion, absence of large ischemic core

Patients randomized to IV tPA alone vs. IV tPA PLUS mechanical thrombectomy using stent retriever

Mechanical thrombectomy to be performed within 6 hrs

Primary outcome: mRS at 90 days

Study stopped early; 39 centers, 196 participants; 98 in each group
SWIFT-PRIME Results

- mRS 2 or less at day 90: 60% vs. 35%
  absolute difference of 25%
- No significant difference in terms of mortality or sICH rates

SWIFT-PRIME

Conclusion:
In patients receiving IV tPA for acute ischemic stroke due to occlusions in the proximal anterior intracranial circulation, thrombectomy with a stent retriever within six hours from symptoms onset improved functional outcome at 90 days

REVASCAT

- Presented this month at European stroke conference, not yet published
- 206 Patients at 4 centers in Spain
- Medical management + intervention with Solitaire vs. medical management alone
- IV TPA failure patients only
- Mechanical thrombectomy within 8 hours

Primary outcome mRS 0-2 at 90 days: 44% vs. 28%
No significant difference in mortality or sICH rates
Insurance Payer Update

- AETNA UPDATE:

Aetna considers endovascular therapy with a retrievable stent medically necessary for persons with acute ischemic stroke who have occlusion of the anterior circulation and evidence of salvageable tissue on imaging, where retrieval is performed within 12 hours after the onset of stroke.


Discussion

- Why current trials were successful
  - Required presence of proximal large vessel occlusion
  - Use of latest technology
  - Faster door to groin puncture and reperfusion times (time is Penumbra)

Discussion

- Grey areas/need further trials/evidence:
  - Very old
  - Patients presenting within 6-12 hrs time window
  - Wake up strokes: need for further trial for window up to 12 hours
  - Stroke effecting posterior circulations
  - Pediatric patients:
OUMC Stroke Program

- Comprehensive stroke center
- Stroke Step-down Unit since 2008
- Neurosciences intensive care unit since: 2009
- Neurointerventional Program since: 2009

- 3 Neurointerventionalists
- 4 Neurointensivists
- 5 Stroke Neurologists
- Stroke Coordinator
- Quality assurance and safety committees

OUMC Stroke Program

- Stroke patients brought in by EMS or transferred from outside hospital

- Streamlined system:
  - Pre-arrival: phone call by EMS or outside ED; time of onset, ETA, IV/PA, stroke team is alerted
  - Upon arrival: stroke code activated; quick evaluation, stat CT/CTA, NI team made aware; if patient qualifies for intervention, quickly moved to Neurointervention suite from CT scanner

OUMC Stroke Program

- Time points documented: (Targets times soon to be implemented)
  - Time of arrival
  - Time to imaging study
  - Time to decision for intervention
  - Time placed on angio-table
  - Time to groin access
  - Time to target vessel catheterized
  - Time to first reperfusion
  - Time to recanalization
Take Home Points

- Rapid treatment is still the most important factor
- Mechanical Thrombectomy within six hours for anterior circulation ischemic strokes secondary to large vessel occlusion now standard of treatment
- Still needs to continue to work on developing better therapies for the rest of the >95% of stroke patients who do not present within time-window

Future:

Thank You!!!