Acute Stroke Intervention State of the Art

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Conflicts

No financial Interest in Any Drugs or Devices in my presentation
Time Window for Treatment

- 0-3 IV therapy
- 0-6 IA therapy
- 0-8 mechanical revascularization

Loosely based on cerebral perfusion data in primates
FIBRINOLYTICS (INTRAVENOUS)

tPA for acute ischemic stroke. NINDS trial

624 patients with ischemic stroke within 3 hours

Intravenous tPA (0.9 mg/kg) vs placebo

Follow-up 3 months

<table>
<thead>
<tr>
<th></th>
<th>tPA</th>
<th>Placebo</th>
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</thead>
<tbody>
<tr>
<td>Improvement at 24 h</td>
<td>47%</td>
<td>39%</td>
</tr>
<tr>
<td>Favorable outcome at 3 m</td>
<td>42%</td>
<td>27%</td>
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<tr>
<td>(Rankin scale)</td>
<td></td>
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<tr>
<td>Intracerebral hemorrhage</td>
<td>6.4%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Death at 3 m</td>
<td>17%</td>
<td>21%</td>
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Patient treated with IV tPA had a relative 30% greater likelihood of having minor or no deficit at 3 months based on Rankin score true for all subgroups
Role for IV tPA
0-3 hours
NIHSS < 12
less severe strokes that present early after onset
Ultrasound-enhanced systemic thrombolysis for acute ischemic stroke
Alexandrov et al NEJM 2004

- 2 MHz TCD focused on occluded intracranial vessel
- 126 patients with acute stroke two groups ultrasound vs placebo
- Complete recanalization or dramatic clinical recovery within two hours
- 49% (31pts) vs 30% 19pts (p=0.03)
- 42% vs 29% 3 month favorable outcome
  - (P=0.2)
Microbubble tPA, TCD
Molina et al stroke Feb 2006

• 38 pts tPA TCD monitoring plus 3 doses of 2.5 g (400 mg/mL) of galactose-based MBs given at 2, 20, and 40 minutes after tPA bolus (MB group).
• Two-hour complete recanalization rate was significantly (P=0.038) higher in the TCD group:
  • tPA/US/MB group (54.5%)
  • tPA/US (40.8%)
  • tPA (23.9%) groups.
3 – 20 % of patients arrive within a 3 hr window
FIBRINOLYTICS (INTRA-ARTERIAL)

Prolyse in Acute Cerebral Thromboembolism (PROACT) II

180 patients with occlusion of middle cerebral artery within 6 hours of onset

Intraarterial Prourokinase (9mg) vs placebo

Follow-up 3 months

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Recanalization</th>
<th>Hemorrhagic transformation</th>
<th>Favorable outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prourokinase</td>
<td>66%</td>
<td>10%</td>
<td>40%</td>
</tr>
<tr>
<td>Placebo</td>
<td>18%</td>
<td>2%</td>
<td>25%</td>
</tr>
</tbody>
</table>
Treated patients had a 60% relative increase in good or excellent outcome Rankin 0-2
EMS BRIDGING TRIAL

• 53% recannalization in the IV/IA tPA group
• 28% IA tPA alone

• No clear difference in outcome between the groups
Minimize reperfusion hemorrhage
Qualitative
or
Quantitative

test of brain tissue viability
PERFUSION IMAGING
MRI
The apparent diffusion coefficient of water is decreased in areas of ischemia.
MRI Diffusion/Perfusion

Kidwell: Stroke, Volume 34:2729-2735, Nov 2003
Magnetic Resonance
TIME
MOTION
RESOLUTION
cerebellum and brainstem
Ischemic Penumbra
Size of Infarct Zone predictive of Intracranial Reperfusion Hemorrhage
Reperfusion Hemorrhage
Outcome Driven by Volume Ratio

Infarct volume

_____________________
Ischemic Penumbra volume
Mechanical Thrombolysis
Concentric Merci Retriever

Thrombus Retriever X5
Basilar Occlusion 24 yr male
NIHSS 16
Basilar Occlusion
Merci Registry

• 141 patients
• 46% female
• Mean Age 67
• Mean Baseline NIHSS 20
• Mean Treatment time approx 4 hrs
Baseline NIH Stroke Scale (n=140*)

- NIHSS 8-10 (4) 3%
- NIHSS 11-20 (76) 54%
- NIHSS >20 (60) 43%

*Baseline NIHSS not recorded for 1 patient
Occlusion Location (n=141)

- ICA (27) 19%
- ICA-T (20) 14%
- MCA (80) 57%
- Vertebal (1) 1%
- Basilar (13) 9%
MERCI TRIAL
RECANNLAIZATION

- Retriever alone   48%
- Retriever plus adjunctive  60%
Good Outcome (90-Day mRS ≤2) By Revascularization Status

- Overall: 28% (36/130)
- Revasc: 46% (29/63)
- Non-Revasc: 10% (7/67)
- Revasc: 45% (35/78)
- Non-Revasc: 2% (1/52)

*p < 0.0001* (ad-hoc analysis using Fisher's Exact Test)
Symptomatic ICH

MERCI 7.8%

PROACT II 10.8%
Overall recanalization rate 79%

- (Thrombolysis in Cerebral Infarction Grade 2 or 3) 79%.

- 8 internal carotid artery terminus
- 7 in the M1/M2 segment
- 4 in the basilar artery.
- 6 deaths
- NIHSS 16 (15-22)
- Survivors NIHSS 5 (2-11)
The Target for Pharmacologic or Mechanic Therapy is the Ischemic Penumbra
Mitochondria
Energy generator of the Cell
Electrons come from burning pyruvate
Steel Energy from Electrons to run the proton pump forming a proton gradient
protons flows back through ATP synthetase and drives ADP to ATP
Energy storage cytochrome c
Cytochrome C

- Copper Center in Cytochrome C has absorption spectra in the near infrared.
  
  Can we make Cytochrome C emit an electron with NIR irradiation?
Switch Fuel Sources pyruvate for an Infrared Photon
Photothera in clinical trails
24 hr window
Stroke Intervention is Expensive
Original DRG for non interventional stroke is approximately $6000.
DRG 559
IV thrombolysis
$11,500
mechanical thrombolysis
DRG 1 and DRG 559
$22,000
Acuity of patient Mix
Conclusion

Perfusion Imaging should guide all stroke intervention. To help minimize symptomatic ICH.
Thank You