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Rapidly Improving or Mild Strokes

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NINDS Trial:

- Patients excluded if rapidly improving or minor symptoms (RIMS)

AHA Guidelines:

- Neurological signs should not be clearing spontaneously
- Neurological signs should not be minor & isolated



What is a minor stroke?

Fischer, et al. (Switzerland) Stroke 2010

760 patients with acute ischemic stroke classified as:

- a) Score ≤ 1 on NIHSS and normal consciousness
 - b) Lacunar-like syndrome
 - c) Motor deficits with or without sensory deficits
 - d) NIHSS ≤ 9 excluding those with aphasia, neglect, or decreased consciousness
 - e) NIHSS ≤ 9
 - f) NIHSS ≤ 3
- Short term outcome favorable when patients discharged home
 - Medium term outcome favorable as mRS ≤ 2 at 3 months

Conclusions:

- Patients fulfilling definitions a) & f) had best short & medium term outcomes;
- Best suited for definition of “minor stroke”



No IV t-PA for RIMS How Often Does This Occur?

Calgary study:

- 314 Ischemic stroke patients came within 3 hours
- 98 (31%) did not receive IV t-PA due to RIMS

Barber et al. Neurology 2001

UCLA Case Series:

- 128 Ischemic stroke patients came within 3 hours
- 41 (34%) did not receive t-PA due to RIMS

Smith, et al. Stroke 2005

Case Series: (Switzerland)

- 876 Ischemic stroke patients came within 24 hours
- 162 (19%) did not receive IV t-PA due to RIMS

Nedeltchev et al. Stroke 2007



No IV t-PA for RIMS How Often Does This Occur? (cont.)

Midwest USA Stroke Registry 2008 data:

- 315 Ischemic stroke patients came within 2 hours
- 76 (24%) did not receive IV t-PA due to RIMS

Large Nationwide Study: (2003- 2009) Canada & US

- 93,517 Ischemic stroke patients from 1092 hospitals came within 2 hours
- 29,200 (31.2%) did not receive IV t-PA due to RIMS

Smith, et al. Stroke 2011



What happens to patients who are
not treated with IV t-PA?



Calgary Study:

- 98 patients did not receive IV t-PA due to RIMS
- 32% of these remained dependent at discharge or died during hospitalization

Barber et al Neurology 2001

UCLA Case Series:

- 41 patients not treated due to RIMS
- 11/41 (27%) died or not discharged home due to worsening (6) or persistent “mild deficit” (5)

Smith et al. Stroke 2005



Midwest USA Stroke Registry Data: (2008)

- 76 patients did not receive t-PA due to RIMS;
 - 69 (91%) ambulated independently prior to the stroke
 - At discharge only 38 (50%) ambulated independently!!

Large nationwide study with RIMS: (2011)

- 29,200 (31.2%) patients did not receive t-PA
 - 28.3% not discharged home
 - 28.5% unable to ambulate without assistance at hospital discharge
- Those not discharged home were more likely to be older, female, black, have higher NIHSS score, vascular risk factors and not taking lipid lowering medication before admission



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Patient outcomes at 3 Months if not treated with IV t-PA



Switzerland case series 162 patients with RIMS:

- Favorable: (122 patients), mRS 0-1; No significant disability
- Unfavorable: (40 patients), mRS > 1
 - 26 patients, mRS 2; Slight disability
 - 12 patients, mRS 3,4; Moderate – moderately severe disability
 - 2 patients, mRS 6; Dead

Nedeltchev Stroke 2007



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What happens to patients who are
treated with IV t-PA?



2006 Switzerland Case Series:

- 19 Patients with rapid improvement were treated at mean NIHSS of 5 (range 1-6)
- 3 Month outcomes:
 - One patient died due to recurrent stroke from AFib
 - NIHSS at 3 months in remaining was 0, mRS range 0-1

Baumann, et al Stroke 2006

2009 Germany Case Series:

- 32 patients (left hemisphere affected in majority, especially aphasia)
- 3 month outcomes:
 - Favorable (mRS 0-1) in 94% of patients
 - 47% recovered without any persisting symptoms
 - Only one asymptomatic and no symptomatic hemorrhage was observed

Köhrmann, et al Cerebrovascular Disease 2009



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Should we treat rapidly
improving or minor stroke?



RIMS that have poor outcomes are a heterogeneous group

- TIA- subsequently have strokes during hospitalization
- Mild strokes- worsen during hospitalization
- NIHSS is not sensitive for gait ataxia & cognitive deficits; therefore leading to a low NIHSS score

Smith et al. Stroke 2005



There was limited data on thrombolysis in the elderly until June, 2012

IST-3 Trial

- Completed trials until IST-3: 94 patients > 80 years in thrombolysis RCT
 - NINDS trial included a few patients over 80 years
 - ECASS-3 did not include patients over 80 years
 - IST-3

IST-3: Lancet June 23,2012

- 3035 patients enrolled up to 6h after acute stroke
 - 1515 given t-PA-726 older than 80 years old
 - 1520 control group



Thrombolysis in Elderly Patients (cont.)

- At 6 months end point, 37% t-PA & 35% control group alive & independent:
 - Fatal or non-fatal intracranial hemorrhage within 7 days occurred in 104 t-PA patients vs. 16 in control group
 - However, between 7 days & 6 months, there were fewer deaths in t-PA group than control group, so that by 6 months, the total number of deaths in both groups were equal with better functional outcomes in the t-PA group.
- Therefore, for the types of patients recruited in IST-3, despite early hazards, thrombolysis within 6 hours of stroke onset improved functional outcome. Benefits were not diminished in the elderly.



Recombinant t-PA for acute ischemic stroke: updated review & meta-analysis: Lancet June 23,2012

- For every 100 patients treated with t-PA up to 6 hours after stroke, 42 more patients were alive and independent (mRS 0-2) at 1 to 6 months. 55 more were alive a favorable outcome (mRS 0-1) at the end of follow up.
- This benefit occurred despite an increase in the number of early symptomatic intracranial hemorrhage and early deaths.



- We need clearer definitions/ exclusion criteria for RIMS escaping the exclusions of the patients from original NINDS Trial 1995 and AHA Guidelines
- We should consider reliable serial NIHSS evaluation before t-PA treatment and periodically thereafter
- NIHSS predicts outcome but not constructed with this specific aim
 - not all stroke signs captured on NIHSS
 - Frequently patients with a low NIHSS score of 3 could represent the deficit of a person with a moderately severe language impairment (disabling stroke) But could also represent mild facial weakness or asymmetry, mild dysarthria and a mild drift of an appear extremity (non-disabling stroke).
 - Perhaps further refinement of NIHSS would help decision making about treatment of RIMS



- We need more data on stroke subtype analysis and outcomes for RIMS
- There is some evidence that large vessel occlusion portends odds of poor outcome
- Early vascular evaluation with advanced imaging will help obtain this information
- In past decade, exploratory studies to assess the safety and efficacy of IV t-PA in RIMS patients have been conducted and generally show good outcomes, some recovering without any persistent symptoms.
 - The overall reported risk of symptomatic intracranial hemorrhage after thrombolysis in RIMS patients was relatively low reinforcing that the benefit of IV t-PA may outweigh the risk in these patients.
 - Treating these mild ischemic stroke patients could reduce the number of patients left disabled and lift a huge economic financial burden on the health system



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Thank you!

