Treatment of Acute Ischemic Stroke

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Daryl R. Gress Professor of Neurocritical Care and Stroke
Disclosures

- Research grant from Boehringer Ingelheim
- Financial compensation Concentric Medical

Wade S. Smith, MD, PhD
Director UCSF Neurovascular Service
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Non-modifiable Factors

- Age
- Stroke Severity
- Stroke Subtype
- Vessel Involved
- Imaging Findings
- Prior TIA/Stroke
- Comorbidities

Modifiable Factors

- Revascularization
- Blood Pressure
- Glucose
- Temperature
- Stroke Unit Care
- Rehabilitation

Imaging

Hemorrhagic?

Ischemic?

Stroke/TIA

Imaging

Risk Factor Modification:
- Antithrombotic
- Statin
- ACE Inhibitor
- Warfarin, or aspirin if contraindicated

Aneurysm?

Hypertensive

ICH?

Other

Investigate for cause

Consider Thrombolysis
Thrombectomy

SAH Management

Risk Factor Modification

ICH Management

Risk Factor Modification

Specific Cause

Management and Treatment

Sinus Thrombosis?

Anticoagulation

Dissection?

Intracranial Atherosclerosis?

Evidenced Based Stroke Treatment
Patient Arrives in CT

Non-contrast CT Head

Positioned

CT Perfusion (40 cc contrast) Twice

CTA brain to chest (70 cc contrast)
Risk of Contrast Nephropathy

N = 2109
Had stroke CT protocol

N = 1075
Included in study

N = 52
Creatinine rise of $\geq 0.5 \text{ mg/dl}$

N = 4
Possible contrast nephropathy

N = 2
Required temporary hemodialysis

0.37%

0.19%

Josephson et al, Neurology (2005) 64:1805
CT angiography
Stroke/TIA → Imaging

Ischemic?

Hemorrhagic?

Evidenced Based Stroke Treatment
Evidenced Based Stroke Treatment
Ischemic?

Consider Thrombolysis Thrombectomy

Atrial Fibrillation, Mechanical Valve, Mural Thrombus?

Carotid Atherosclerosis?

Small Vessel?

Intracranial Atherosclerosis?

Sinus Thrombosis, Dissection?

Sickle Cell Disease

Other

Warfarin, or aspirin if contraindicated

CEA or Stent

Risk Factor Modification:
- Antithrombotic
- Statin
- ACE Inhibitor

Risk Factor Modification:

Anticoagulation

Transfusion, Bone Marrow Tx

Treat specific cause, consultation
ECASS-III

Randomized, Controlled

NINDS

PROACT

Prospective, Non-randomized

IMS-I, IMS-II

MERCI, Multi MERCI, Penumbra

0 hours 3 4.5 6 8 12
ECASS-III

Randomized, Controlled

NINDS

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0 hours

3

4.5

6

8

12
NINDS t-PA Ischemic Stroke

- Intravenous t-PA vs. placebo (N=312 each group)
  - 0.9 mg/kg t-PA IV (10% bolus, 1 hr infusion)
- within 90 mins and 180 mins of symptom onset
- CT exclude hemorrhage

- symptomatic intracranial hemorrhage
  - 6% vs. 0.6% (t-PA vs. placebo)
- 3% hemorrhage related death

ECASS-III

NINDS

0 hours

PROACT

3

4.5

6

8

12

Randomized, Controlled

Prospective, Non-randomized

IMS-I, IMS-II

MERCI, Multi MERCI, Penumbra
ECASS-III

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0 hours

3

4.5

6

8

12
**Table 1. Major Inclusion and Exclusion Criteria.**

**Main inclusion criteria**
- Acute ischemic stroke
- Age, 18 to 80 years
- Onset of stroke symptoms 3 to 4.5 hours before initiation of study-drug administration
- Stroke symptoms present for at least 30 minutes with no significant improvement before treatment

**Main exclusion criteria**
- Intracranial hemorrhage
- Time of symptom onset unknown
- Symptoms rapidly improving or only minor before start of infusion
- Severe stroke as assessed clinically (e.g., NIHSS score >25) or by appropriate imaging techniques *
- Seizure at the onset of stroke
- Stroke or serious head trauma within the previous 3 months
- Combination of previous stroke and diabetes mellitus
- Administration of heparin within the 48 hours preceding the onset of stroke, with an activated partial-thromboplastin time at presentation exceeding the upper limit of the normal range
- Platelet count of less than 100,000 per cubic millimeter
- Systolic pressure greater than 185 mm Hg or diastolic pressure greater than 110 mm Hg, or aggressive treatment (intravenous medication) necessary to reduce blood pressure to these limits
- Blood glucose less than 50 mg per deciliter or greater than 400 mg per deciliter
- Symptoms suggestive of subarachnoid hemorrhage, even if CT scan was normal
- Oral anticoagulant treatment
- Major surgery or severe trauma within the previous 3 months
- Other major disorders associated with an increased risk of bleeding

* A severe stroke as assessed by imaging was defined as a stroke involving more than one third of the middle cerebral-artery territory. NIHSS denotes National Institutes of Health Stroke Scale in which total scores range from 0 to 42, with higher values reflecting more severe cerebral infarcts.
## ECASS-III

### Table 3. Odds Ratios for Primary End Point and Secondary End Point, Including Components, in the Intention-to-Treat and Per-Protocol Populations at 90 Days.※

<table>
<thead>
<tr>
<th>End Point</th>
<th>Intention-to-Treat Population</th>
<th>Per-Protocol Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alteplase Group (N=418) no. (%)</td>
<td>Placebo Group (N=403) no. (%)</td>
</tr>
<tr>
<td><strong>Primary end point</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS score of 0 or 1 — unadjusted analysis</td>
<td>219 (52.4)</td>
<td>182 (45.2)</td>
</tr>
<tr>
<td>mRS score of 0 or 1 — adjusted analysis‡</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Secondary end point</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global outcome¶</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS score of 0 or 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barthel Index score ≥95**</td>
<td>265 (63.4)</td>
<td>236 (58.6)</td>
</tr>
<tr>
<td>NIHSS score of 0 or 1††</td>
<td>210 (50.2)</td>
<td>174 (43.2)</td>
</tr>
<tr>
<td>GOS score of 1‡‡†</td>
<td>213 (51.0)</td>
<td>183 (45.4)</td>
</tr>
</tbody>
</table>

* GOS denotes Glasgow Outcome Scale, mRS modified Rankin scale, NIHSS National Institutes of Health Stroke Scale, and NINDS National Institute of Neurological Disorders and Stroke.
† P value was obtained by the Pearson chi-square test of proportions.
‡ This analysis was adjusted for NIHSS score at presentation and the time to start of treatment.
§ P value was obtained by stepwise logistic regression.
¶ The global outcome analysis is a multidimensional calculation of a favorable outcome, defined by several individual outcome scales and entered into a statistical algorithm. This statistical approach is a global odds-ratio test based on a linear logistic-regression model (a method that uses generalized estimation equations to perform a Wald-type test). No percentages can be given owing to the underlying statistical method. The global odds ratio is the probability of a favorable outcome with alteplase as compared with placebo.
|| Scores on the modified Rankin scale range from 0 (no symptoms at all) to 6 (death).
** The Barthel Index assesses the ability to perform activities of daily living on a scale that ranges from 0 (complete dependence on help with activities of daily living) to 100 (independence).
†† Scores on the NIHSS range from 0 to 42, with higher values reflecting more severe neurologic impairment (<5, mild impairment; ≥25, very severe impairment).
‡‡ The Glasgow Outcome Scale is a 5-point scale on which 1 indicates independence, 3 severe disability, and 5 death.

60 hours

Randomized, Controlled

NINDS

PROACT

ECASS-III

0 hours 3 4.5 6 8 12

Prospective, Non-randomized

IMS-I, IMS-II

MERCI, Multi MERCI, Penumbra
Intraarterial Thrombolysis
PROACT-II: mRS ≤ 2

Patients mRS 0-2 (%)

Baseline NIHSS

Placebo  r-ProUK

63 63

* OR 2.13 (1.02-4.42), p=0.043

Randomized, Controlled

Prospective, Non-randomized

0 hours

NINDS

ECASS-III

PROACT

IMS-I, IMS-II

MERCI, Multi MERCI, Penumbra
IMS-II AOL Recanalization to Grade 3

EKOS Primo w/US vs Standard + EKOS no US vs. IMS I Standard
(M3,4 Excluded)

68.9% vs 53.3%**

41.4% vs 30%*

EKOS US n=26
IMS II No US n=14
IMS I n=23
IMS I n=60

*P=0.41
**P=0.08
ECASS-III

Randomized, Controlled

NINDS

Prospective, Non-randomized

PROACT

IMS-I, IMS-II

MERCI, Multi MERCI, Penumbra

0 hours

3

4.5

6

8

12
Safety and Efficacy of Mechanical Embolectomy in Acute Ischemic Stroke
Results of the MERCI Trial

Wade S. Smith, MD, PhD; Gene Sung, MD; Sidney Starkman, MD; Jeffrey L. Saver, MD; Chelsea S. Kidwell, MD; Y. Pierre Gobin, MD; Helmi L. Lutsep, MD; Gary M. Nesbit, MD; Thomas Grobelny, MD; Marilyn M. Rymer, MD; Isaac E. Silverman, MD; Randall T. Higashida, MD; Ronald F. Budzik, MD; Michael P. Marks, MD; for the MERCI Trial Investigators

Stroke (2005) 36:1432
Patients Screened (n=1809)

Patients Enrolled (n=151)

Device Deployed (n=141)
- Recanalization: 48% (68/141)
- Complications: 7.1% (10/141)
- Symp ICH: 7.8% (11/141)
- mRS ≤ 2: 28% (36/130)
- Mortality: 44% (60/138)

Retriever Alone (n=90)
- Recanalization: 57% (51/90)
- Complications: 10% (9/90)
- Symp ICH: 7.8% (7/90)
- mRS ≤ 2: 28% (23/83)
- Mortality: 40% (36/89)

Retriever & Adjuvant (n=51)
- Recanalization: 33% (17/51)
- Complications: 2% (1/51)
- Symp ICH: 7.8% (4/51)
- mRS ≤ 2: 28% (13/47)
- Mortality: 48% (24/50)

Stroke (2005) 36:1432
MERCI Clinical Outcomes

Good Outcome Mortality (90 day)

- Recanalized: 46%
- Not Recanalized: 10.4%

Mortality (90 day)

- Recanalized: 31.8%
- Not Recanalized: 54.2%

Significance:

- Recanalized vs. Not Recanalized: $p < 0.0001$
- Mortality vs. Not Mortality: $p = 0.003$
## TABLE 4. Multivariate Predictors of Good Outcome and Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>mRS ≤ 2</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Revascularization</td>
<td>12.82 (2.95–55.75)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age, y, decade</td>
<td>0.94 (0.90–0.98)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Baseline NIHSS</td>
<td>0.78 (0.67–0.89)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Procedure time, hr</td>
<td>0.36 (0.17–0.78)</td>
<td>0.0077</td>
</tr>
<tr>
<td>Right brain infarct</td>
<td>0.14 (0.04–0.52)</td>
<td>0.0041</td>
</tr>
</tbody>
</table>
Mechanical Thrombectomy for Acute Ischemic Stroke
Final Results of the Multi MERCI Trial

Wade S. Smith, MD, PhD; Gene Sung, MD, MPH; Jeffrey Saver, MD; Ronald Budzik, MD; Gary Duckwiler, MD; David S. Liebeskind, MD; Helmi L. Lutsep, MD; Marilyn M. Rymer, MD; Randall T. Higashida, MD; Sidney Starkman, MD; Y. Pierre Gobin, MD
for the Multi MERCI Investigators

<table>
<thead>
<tr>
<th>Site of Occlusion</th>
<th>Posterior</th>
<th>ICA-T</th>
<th>MCA-M1</th>
<th>MCA-M2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior</td>
<td>N=8 L5</td>
<td>N=41 L5</td>
<td>N=67 L5</td>
<td>N=15 L5</td>
</tr>
<tr>
<td>Device</td>
<td>N=14 All</td>
<td>N=52 All</td>
<td>N=77 All</td>
<td>N=21 All</td>
</tr>
<tr>
<td>Age mean, y</td>
<td>L5</td>
<td>60</td>
<td>69</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>62</td>
<td>67</td>
<td>70</td>
</tr>
<tr>
<td>Baseline median NIHSS</td>
<td>L5</td>
<td>17</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>19</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>Post Retriever Recanalization, %</td>
<td>L5</td>
<td>88</td>
<td>59</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>71</td>
<td>52</td>
<td>48</td>
</tr>
<tr>
<td>Final Recanalization, %</td>
<td>L5</td>
<td>100</td>
<td>71</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>86</td>
<td>65</td>
<td>61</td>
</tr>
<tr>
<td>Favorable outcome (mRS ≤ 2), %</td>
<td>L5</td>
<td>38</td>
<td>33</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>29</td>
<td>33</td>
<td>36</td>
</tr>
<tr>
<td>Mortality, %</td>
<td>L5</td>
<td>38</td>
<td>48</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>43</td>
<td>45</td>
<td>29</td>
</tr>
<tr>
<td>Symptomatic Hemorrhage, %</td>
<td>L5</td>
<td>13</td>
<td>9.8</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>29</td>
<td>7.7</td>
<td>9.1</td>
</tr>
<tr>
<td>Symptomatic PH-2 Hemorrhage, %</td>
<td>L5</td>
<td>0</td>
<td>2.4</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>0</td>
<td>1.9</td>
<td>3.9</td>
</tr>
</tbody>
</table>
L5 vs. X5/X6

- **Device Recanalization**: MERCI 48.2%, Multi MERCI L5 57.3%
- **Final Recanalization**: MERCI 60.3%, Multi MERCI L5 69.5%
Table 5. Use of IV or IA thrombolitics

<table>
<thead>
<tr>
<th>Result</th>
<th>IV t-PA N=48</th>
<th>No IV t-PA N=116</th>
<th>P</th>
<th>IA lytic N=57</th>
<th>No IA lytic N=107</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recanalization Post Retriever, %</td>
<td>58</td>
<td>53</td>
<td>0.61</td>
<td>33</td>
<td>66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recanalization Post Adjuvant, %</td>
<td>73</td>
<td>66</td>
<td>0.46</td>
<td>68</td>
<td>68</td>
<td>0.99</td>
</tr>
<tr>
<td>Symptom onset to arterial puncture, hr</td>
<td>3.9</td>
<td>4.6</td>
<td>0.031</td>
<td>3.7</td>
<td>4.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IA lytic usage, %</td>
<td>35</td>
<td>34</td>
<td>0.99</td>
<td>100</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>mRS ≤ 2 at 90 days, %</td>
<td>38</td>
<td>35</td>
<td>0.72</td>
<td>32</td>
<td>39</td>
<td>0.49</td>
</tr>
<tr>
<td>Mortality at 90 days, %</td>
<td>28</td>
<td>36</td>
<td>0.36</td>
<td>43</td>
<td>29</td>
<td>0.08</td>
</tr>
<tr>
<td>Intracranial Hemorrhage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic ICH, %</td>
<td>10</td>
<td>9.5</td>
<td>0.99</td>
<td>14</td>
<td>7.5</td>
<td>0.27</td>
</tr>
<tr>
<td>Symptomatic PH-2, %</td>
<td>2.1</td>
<td>2.6</td>
<td>0.99</td>
<td>3.5</td>
<td>1.9</td>
<td>0.61</td>
</tr>
<tr>
<td>Clinically sig. proc. complications, %</td>
<td>4.2</td>
<td>6.0</td>
<td>0.99</td>
<td>12</td>
<td>1.9</td>
<td>0.009</td>
</tr>
</tbody>
</table>
Multi MERCI Clinical Outcomes

Revascularized

Non-revascularized

0 1 2 3 4 5 6 mRS

49% 26% 25%

9.6% 38% 52%

0% 50% 100%
Penumbra Device

- Aspiration catheter
- Clot maceration device
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean) years</td>
<td>63.5</td>
</tr>
<tr>
<td>Baseline NIHSS (mean)</td>
<td>17.5</td>
</tr>
<tr>
<td>Groin access (mean) hrs</td>
<td>4.1</td>
</tr>
<tr>
<td>Revascularization</td>
<td>82%</td>
</tr>
<tr>
<td>90-d mRS ≤ 2, overall</td>
<td>25%</td>
</tr>
</tbody>
</table>

†ISC, 2008
## Comparison MERCI/Penumbra

<table>
<thead>
<tr>
<th></th>
<th>Merci</th>
<th>Multi Merci</th>
<th>Penumbra</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>33%</td>
<td>32%</td>
<td>18%</td>
</tr>
<tr>
<td>MCA</td>
<td>57%</td>
<td>60%</td>
<td>70%</td>
</tr>
<tr>
<td>Vert-Basilar</td>
<td>10%</td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td>TIMI 2</td>
<td>24%</td>
<td>19%</td>
<td>54%</td>
</tr>
<tr>
<td>TIMI 3</td>
<td>24%</td>
<td>49%</td>
<td>27%</td>
</tr>
</tbody>
</table>
89 year old woman
LSN 3 PM
L MCA syndrome
Imaging at 7:20 PM
Unable to open MCA Imaging 3 days later

Day 0 MTT
## Comparison of Major Endovascular Trials

<table>
<thead>
<tr>
<th></th>
<th>Recanalization</th>
<th>Outcome (mRS ≤ 2)</th>
<th>Mortality</th>
<th>Symptomatic ICH</th>
<th>Baseline NIHSS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rx</td>
<td>Cont</td>
<td>Rx</td>
<td>Cont</td>
<td>Rx</td>
</tr>
<tr>
<td>PROACT-II N=180</td>
<td>66%</td>
<td>18%</td>
<td>40%</td>
<td>25%</td>
<td>25%</td>
</tr>
<tr>
<td>IMS-I N=80</td>
<td>56%</td>
<td>.</td>
<td>43%</td>
<td>.</td>
<td>16%</td>
</tr>
<tr>
<td>IMS-II N=73</td>
<td>58%</td>
<td>.</td>
<td>45%</td>
<td>.</td>
<td>16%</td>
</tr>
<tr>
<td>MERCI N=151</td>
<td>60%</td>
<td>.</td>
<td>28%</td>
<td>.</td>
<td>44%</td>
</tr>
<tr>
<td>Multi-MERCI I N=164</td>
<td>69%</td>
<td>.</td>
<td>36%</td>
<td>.</td>
<td>34%</td>
</tr>
<tr>
<td>Penumbra N=125</td>
<td>82%</td>
<td>24%</td>
<td>33%</td>
<td>.</td>
<td>11%</td>
</tr>
</tbody>
</table>
Comparison: Recanalization vs. Non-Recanalization

Outcome: Good Outcome by Time

<table>
<thead>
<tr>
<th>Study</th>
<th>Recanalization n/N</th>
<th>Non-Recanalization n/N</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>von Kummer 1991</td>
<td>8/12</td>
<td>3/9</td>
<td>2.9</td>
<td>3.57[0.66,19.33]</td>
<td></td>
</tr>
<tr>
<td>Mohan 1991</td>
<td>6/16</td>
<td>0/4</td>
<td>1.8</td>
<td>6.19[0.63,61.08]</td>
<td></td>
</tr>
<tr>
<td>Castlo 1992</td>
<td>4/4</td>
<td>0/1</td>
<td>0.3</td>
<td>14.6[1.11,190.30]</td>
<td></td>
</tr>
<tr>
<td>Endo 1998</td>
<td>4/8</td>
<td>0/13</td>
<td>1.7</td>
<td>21.9[4.2,195.50]</td>
<td></td>
</tr>
<tr>
<td>Lewandowsi 1999</td>
<td>9/14</td>
<td>2/8</td>
<td>2.9</td>
<td>4.4[0.62,34.47]</td>
<td></td>
</tr>
<tr>
<td>Alexandrov 2001</td>
<td>15/43</td>
<td>1/22</td>
<td>5.9</td>
<td>5.0[1.53,16.33]</td>
<td></td>
</tr>
<tr>
<td>Molina 2002</td>
<td>11/17</td>
<td>2/15</td>
<td>4.3</td>
<td>7.6[1.96,31.65]</td>
<td></td>
</tr>
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<td>Subtotal(95%CI)</td>
<td>57/112</td>
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Test for heterogeneity chi-square=3.65 df=6 p=0.72

Test for overall effect z=5.58 p=0.00001

<table>
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<tr>
<th>Study</th>
<th>Recanalization n/N</th>
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<td>del Zoppo 1988</td>
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<td>Lee 1994</td>
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<td>Sasaki 1995</td>
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<td>von Kummer 1995</td>
<td>12/22</td>
<td>12/55</td>
<td>5.3</td>
<td>4.6[1.6,16.49]</td>
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<td>Gonner 1998</td>
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<td>6/16</td>
<td>0.5</td>
<td>6.2[0.12,32.04]</td>
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<td>Edwards 1999</td>
<td>5/10</td>
<td>0/1</td>
<td>3.4</td>
<td>4.9[1.23,16.24]</td>
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<tr>
<td>Jahan 1999</td>
<td>7/11</td>
<td>3/15</td>
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<td>6.8[1.18,39.33]</td>
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<td>Schalling 2000</td>
<td>9/11</td>
<td>3/9</td>
<td>1.9</td>
<td>4.0[0.51,31.85]</td>
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<td>Ernst 2000</td>
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<td>2/5</td>
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<td>5/17</td>
<td>3/5</td>
<td>1.3</td>
<td>2.4[0.02,2.65]</td>
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<td>Qureshi 2002</td>
<td>5/16</td>
<td>2/3</td>
<td>1.2</td>
<td>4.2[0.30,7.27]</td>
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<td>Uno 2002</td>
<td>5/7</td>
<td>1/3</td>
<td>1.2</td>
<td>7.9[4.45,01,1260.13]</td>
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<td>Yoneyama 2002</td>
<td>11/12</td>
<td>0/3</td>
<td>3.7</td>
<td>2.0[0.12,3.60]</td>
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<tr>
<td>Hirasawa 2002</td>
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<td>2/5</td>
<td>2.7</td>
<td>6.8[1.18,39.33]</td>
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<td>13/24</td>
<td>1.1</td>
<td>4.7[1.23,9.51]</td>
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<tr>
<td>Zaidi 2002</td>
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<td>1/7</td>
<td>2.2</td>
<td>3.7[0.53,26.53]</td>
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<tr>
<td>Rother 2002</td>
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<td>38/69</td>
<td>0.3</td>
<td>4.0[2.54,0.60]</td>
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Subtotal(95%CI) 260/447 101/367

Test for heterogeneity chi-square=31.62 df=25 p=0.17

Test for overall effect z=8.55 p=0.00001

<table>
<thead>
<tr>
<th>Study</th>
<th>Recanalization n/N</th>
<th>Non-Recanalization n/N</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total(95%CI)</td>
<td>325/559</td>
<td>109/439</td>
<td>100.0</td>
<td>4.4[3.32,9.91]</td>
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</tbody>
</table>

Test for heterogeneity chi-square=36.77 df=32 p=0.26

Test for overall effect z=10.14 p=0.00001

Figure 2. Relationship of recanalization vs nonrecanalization to good outcome at 3 months.
Conclusions

• Large vessel stroke is highly morbid
• IV thrombolytics are poorly effective for large vessel stroke
• IA lysis improves clinical outcome (in M1 occlusions)
• Mechanical thrombectomy opens vessels 48-82% of the time and adjuvant IA lysis improves final recanalization to 60-69%
• Better outcome is associated with recanalization
• Randomized data is lacking
Future

- IMS-III Trial ongoing: 3 hour window
  - Is going to the angio suite better than medical therapy for patients within 3 hours of stroke onset?

- MR-RESCUE: 3-6 hour window
  - In patients with PWI/DWI mismatch, does mechanical embolectomy improve outcome?

- RETRIEVE: 0-8 hour window
  - Does mechanical embolectomy +/- IA lysis achieve better outcomes than medical therapy alone (IV t-PA allowed)
Ischemic?

Consider Thrombolysis Thrombectomy

Consider Hemicraniectiony

### Atrial Fibrillation, Mechanical Valve, Mural Thrombus?

- Warfarin, or aspirin if contraindicated

### Carotid Atherosclerosis?

- CEA or Stent

### Small Vessel?

### Intracranial Atherosclerosis?

### Sinus Thrombosis, Dissection?

- Anticoagulation

### Sickle Cell Disease

- Transfusion, Bone Marrow Tx

### Other

**Risk Factor Modification:**
- Antithrombotic
- Statin
- ACE Inhibitor

**Treat specific cause, consultation**
Hemicraniectomy

- **Conservative treatment**
  - MRS=2: 2% (1/42)
  - MRS=3: 19% (8/42)
  - MRS=4: 2% (1/42)
  - MRS=5: 5% (2/42)
  - Death: 71% (30/42)

- **Surgery**
  - MRS=2: 14% (7/51)
  - MRS=3: 29% (15/51)
  - MRS=4: 31% (16/51)
  - MRS=5: 4% (2/51)
  - Death: 22% (11/51)
<table>
<thead>
<tr>
<th>Outcome/patients</th>
<th>Conservative</th>
<th>Surgery</th>
<th>ARR (%)</th>
<th>95% CI</th>
<th>OR</th>
<th>95% CI</th>
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<tr>
<td>mRS&gt;4 at 12 months</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DECIMAL</td>
<td>14/18</td>
<td>5/20</td>
<td>52.8</td>
<td>25.8 to 79.8</td>
<td>0.10</td>
<td>0.02 to 0.43</td>
</tr>
<tr>
<td>DESTINY</td>
<td>10/15</td>
<td>4/17</td>
<td>43.1</td>
<td>11.9 to 74.4</td>
<td>0.15</td>
<td>0.03 to 0.73</td>
</tr>
<tr>
<td>HAMLET</td>
<td>8/9</td>
<td>4/14</td>
<td>60.3</td>
<td>29.0 to 91.6</td>
<td>0.05</td>
<td>0.00 to 0.54</td>
</tr>
<tr>
<td>Total</td>
<td>32/42</td>
<td>13/51</td>
<td>51.2</td>
<td>33.9 to 68.5</td>
<td>0.10</td>
<td>0.04 to 0.27</td>
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<tr>
<td>Significance: p&lt;0.0001</td>
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<tr>
<td>Heterogeneity: p=0.74</td>
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<tr>
<td>mRS&gt;3 at 12 months</td>
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<tr>
<td>DECIMAL</td>
<td>14/18</td>
<td>10/20</td>
<td>27.8</td>
<td>-1.4 to 56.9</td>
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<td>0.07 to 1.18</td>
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<td>DESTINY</td>
<td>11/15</td>
<td>9/17</td>
<td>20.4</td>
<td>-12.2 to 53.0</td>
<td>0.41</td>
<td>0.09 to 1.81</td>
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<td>10/14</td>
<td>17.5</td>
<td>-13.9 to 48.8</td>
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<td>0.03 to 3.38</td>
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<tr>
<td>Total</td>
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<td>29/51</td>
<td>22.7</td>
<td>4.6 to 40.9</td>
<td>0.33</td>
<td>0.13 to 0.86</td>
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<td>Significance: p=0.014</td>
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<td>Heterogeneity: p=0.89</td>
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<tr>
<td>Death at 12 months</td>
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<td></td>
</tr>
<tr>
<td>DECIMAL</td>
<td>14/18</td>
<td>5/20</td>
<td>52.8</td>
<td>25.8 to 79.8</td>
<td>0.10</td>
<td>0.02 to 0.43</td>
</tr>
<tr>
<td>DESTINY</td>
<td>8/15</td>
<td>3/17</td>
<td>35.7</td>
<td>4.6 to 66.8</td>
<td>0.19</td>
<td>0.04 to 0.94</td>
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<tr>
<td>HAMLET</td>
<td>8/9</td>
<td>3/14</td>
<td>67.5</td>
<td>37.7 to 97.2</td>
<td>0.03</td>
<td>0.00 to 0.39</td>
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<tr>
<td>Total</td>
<td>30/42</td>
<td>11/51</td>
<td>50.3</td>
<td>33.3 to 67.4</td>
<td>0.10</td>
<td>0.04 to 0.27</td>
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<tr>
<td>Significance: p&lt;0.0001</td>
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</table>
No aphasia
DECIMAL 5/7 1/8 58.9 18.4 to 99.5 0.06 0.00–0.82
DESTINY 3/4 2/7 46.4 –7.6 to 100.5 0.13 0.01–2.18
HAMLET 6/6 2/8 65.1 30.1 to 100.0 0.03 0.00–0.74
Total 14/17 5/23 58.2 34.1 to 82.3 0.06 0.01–0.31
Significance: p<0.0001
Heterogeneity: p=0.85

Aphasia
DECIMAL 9/11 4/12 48.5 13.4 to 83.6 0.11 0.02–0.78
DESTINY 7/11 2/10 43.6 5.9 to 81.4 0.14 0.02–1.03
HAMLET 2/3 2/6 33.3 –32.0 to 98.7 0.25 0.01–4.73
Total 18/25 8/28 44.2 20.2 to 68.1 0.14 0.04–0.50
Significance: p=0.0003
Heterogeneity: p=0.92
* CT, CTA (chest through brain), CTP, post-contrast CT
Conclusions

Primary Stroke Center

- IV t-PA
- Medical Support
- ± Imaging Guidance

Comprehensive Stroke Center

- IV and IA techniques
- Image Guidance
- Neurosurgical support (hemicraniectomy)
Treatment: Medical Management

• Airway

• Blood pressure
  – t-PA limit 185/110
  – Lower BP by 15% if exceeds 220/120
  – Choice of BP agent is controversial; labetolol, nicardipine don’t raise ICP

• Temperature
  – Treat fever with antipyretics
  – Cooling blankets, endovascular treatments not proven to change outcome
  – Hypothermia is experimental at present
Treatment: Medical Management

• Glucose
  – Treat hypoglycemia immediately
  – Keep serum glucose < 140 mg/dL
  – Infusion vs. sliding scale insulin is controversial

• DVT Prophylaxis
  – Compression devices unless DVT present
  – Both SQ unfractioned heparin and LMWH are safe and effective to prevent venous clot and likely PE
Treatment:
Medical Management

• Nutrition
  – Assess and document swallowing
  – Discourage rule of NPO X 24 hour as a standard
  – NG tube is preferred if swallowing is unsafe
  – Start feeds as soon as possible
Treatment:
Medical Management

• Brain Edema
  – Posterior fossae strokes should be treated with suboccipital decompression if brainstem is compressed
  – Hemicraniectomy for hemispheric stroke is proven to reduce morality and improve outcomes (Level 1 evidence)
  – Mannitol and hyperventilation not validated but are important bridges to surgical interventions as necessary
  – Follow Na⁺
  – No indication for corticosteroids
Treatment: Medical Management

• Acute Anticoagulation
  – Avoid routine use of heparin
  – Aspirin alone is the only proven strategy within the first 24-48 hours
  – Dural sinus thrombosis and arterial dissection may specifically benefit from heparin

• Induced hypertension: investigational
Adams, H.P., Jr., et al., *Guidelines for the early management of adults with ischemic stroke*: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

UCSF Acute Stroke Protocol

* CT. CTA (chest through brain), CTP, post-contrast CT
Ischemic?

- Consider Thrombolysis Thrombectomy
- Consider Hemicraniectomy

**Atrial Fibrillation, Mechanical Valve, Mural Thrombus?**
- Warfarin, or aspirin if contraindicated
- Risk Factor Modification

**Carotid Atherosclerosis?**
- CEA or Stent

**Small Vessel?**

**Intracranial Atherosclerosis?**

**Sinus Thrombosis, Dissection?**
- Anticoagulation

**Sickle Cell Disease**
- Transfusion, Bone Marrow Tx

**Other**

Risk Factor Modification:
- Antithrombotic
- Statin
- ACE Inhibitor

Treat specific cause, consultation
## Frequency of Stroke by Type

<table>
<thead>
<tr>
<th>Stroke Subtype</th>
<th>Estimated Frequency</th>
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<tr>
<td><strong>Hemorrhage</strong></td>
<td>15%</td>
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<tr>
<td><strong>Ischemic Stroke</strong></td>
<td>85%</td>
</tr>
<tr>
<td>Lacunar (small vessel) stroke</td>
<td>25%</td>
</tr>
<tr>
<td>Cardiogenic embolism</td>
<td>20%</td>
</tr>
<tr>
<td>Artery-artery embolism</td>
<td>15%</td>
</tr>
<tr>
<td>Cryptogenic stroke</td>
<td>30%</td>
</tr>
<tr>
<td>Other Causes</td>
<td>10%</td>
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</table>
Atrial Fibrillation, Mechanical Valve, Mural Thrombus? → Warfarin, or aspirin if contraindicated → Risk Factor Modification
Stroke: Atrial Fibrillation

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Target</th>
<th>Control</th>
<th>Warfarin</th>
<th>P value</th>
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<tr>
<td>AFASAK</td>
<td>671</td>
<td>INR 2.8-4.2</td>
<td>5.5</td>
<td>2.0</td>
<td>&lt; 0.05</td>
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<tr>
<td>BAATAF</td>
<td>420</td>
<td>PTR 1.2-1.5</td>
<td>3.0†</td>
<td>0.41†</td>
<td>&lt; 0.002</td>
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<tr>
<td>SPAF</td>
<td>421</td>
<td>PTR 1.3-1.8</td>
<td>7.4</td>
<td>2.3</td>
<td>&lt; 0.01</td>
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<tr>
<td>CAFA</td>
<td>378</td>
<td>INR 2.0-3.0</td>
<td>5.2†</td>
<td>3.5†</td>
<td>= 0.17</td>
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<tr>
<td>SPINAF</td>
<td>525</td>
<td>PTR 1.2-1.5</td>
<td>4.3†</td>
<td>0.9†</td>
<td>&lt; 0.001</td>
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</table>

† end point stroke only
Usage of Oral Anticoagulation in Patients with Atrial Fibrillation

- Retrospective chart review, Orange & Los Angeles Counties, 1995
- 240 patients, chronic atrial fibrillation, no contraindications for warfarin

CMRI, 1995
Stroke: Atrial Fibrillation

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk Factors†</th>
<th>Recommendation</th>
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<tbody>
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<td>Age &lt; 65</td>
<td>One or more</td>
<td>Warfarin INR 2-3</td>
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<tr>
<td></td>
<td>No risk factors</td>
<td>ASA or no treatment</td>
</tr>
<tr>
<td>Age 65-75</td>
<td>Risk Factors</td>
<td>Warfarin INR 2-3</td>
</tr>
<tr>
<td></td>
<td>No risk factors</td>
<td>Warfarin INR 2-3 or ASA</td>
</tr>
<tr>
<td>Age &gt;75</td>
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<td>Warfarin INR 2-3</td>
</tr>
</tbody>
</table>

† Risk Factors include previous TIA or stroke, hypertension, heart failure, diabetes, clinical coronary artery disease, mitral stenosis, prosthetic heart valves, or thyrotoxicosis
Carotid Atherosclerosis?  ➔  CEA or Stent

Any ipsilateral stroke per year

<table>
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<th>Medical</th>
<th>Surgical</th>
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<td>Symptomatic</td>
<td>18%</td>
<td>4.5%</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>2.2%</td>
<td>1.0%</td>
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</tbody>
</table>

NASCET, 1991

Risk Factor Modification:
- Antithrombotic
- Statin
- ACE Inhibitor

ACAS, 1995
### Table 3. Cumulative Incidence of Adverse Events within One Year.

<table>
<thead>
<tr>
<th>Event</th>
<th>Intention-to-Treat Analysis</th>
<th>Actual-Treatment Analysis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Stenting (N=167)</td>
<td>Endarterectomy (N=167)</td>
</tr>
<tr>
<td></td>
<td>no. (%)</td>
<td>no. (%)</td>
</tr>
<tr>
<td>Death</td>
<td>12 (7.4)</td>
<td>21 (13.5)</td>
</tr>
<tr>
<td>Stroke</td>
<td>10 (6.2)</td>
<td>12 (7.9)</td>
</tr>
<tr>
<td>Major ipsilateral</td>
<td>1 (0.6)</td>
<td>5 (3.3)</td>
</tr>
<tr>
<td>Major nonipsilateral</td>
<td>1 (0.6)</td>
<td>2 (1.4)</td>
</tr>
<tr>
<td>Minor ipsilateral</td>
<td>6 (3.7)</td>
<td>3 (2.0)</td>
</tr>
<tr>
<td>Minor nonipsilateral</td>
<td>3 (1.9)</td>
<td>4 (2.7)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>5 (3.0)</td>
<td>12 (7.5)</td>
</tr>
<tr>
<td>Q-wave</td>
<td>0</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Non–Q-wave</td>
<td>5 (3.0)</td>
<td>10 (6.2)</td>
</tr>
<tr>
<td>Cranial-nerve palsy</td>
<td>0</td>
<td>8 (4.9)</td>
</tr>
<tr>
<td>Target-vessel revascularization</td>
<td>1 (0.6)</td>
<td>6 (4.3)</td>
</tr>
<tr>
<td>Conventional end point (stroke or death at 30 days plus ipsilateral stroke or death from neurologic causes within 31 days to 1 yr)</td>
<td>9 (5.5)</td>
<td>13 (8.4)</td>
</tr>
<tr>
<td>Primary end point (death, stroke, or myocardial infarction at 30 days plus ipsilateral stroke or death from neurologic causes within 31 days to 1 yr)</td>
<td>20 (12.2)</td>
<td>32 (20.1)</td>
</tr>
</tbody>
</table>
Small Vessel?

Risk Factor Modification:
- Antithrombotic
- Statin
- ACE Inhibitor
Small Vessel Stroke

- Lenticulostriate
- Thalamoperforators
- Brainstem penetrators
- Cerebellar hemisphere
- Deep cerebral white matter
Fig. 7.13  (a) A complex vascular coil from a hypertensive patient who died of an ICH visualized in 1000 μm celloidin sections reacted for alkaline phosphatase. (b) High resolution microradiograph of a similarly reacted section of 500 μm thickness shows an arteriolar knot-like structure. (a: from ref. 91, with permission; b: from ref. 92, with permission.)
## Stroke Risk Factors

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>1.16</td>
<td>4.0</td>
<td>&gt; 40%</td>
<td>Yes</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>2.0</td>
<td>2.2</td>
<td>15-40%</td>
<td>No</td>
</tr>
<tr>
<td>LVH</td>
<td>2.2</td>
<td>2.2</td>
<td>15-40%</td>
<td>No</td>
</tr>
<tr>
<td>CHF</td>
<td>2.4</td>
<td>1.7</td>
<td>&lt;15%</td>
<td>No</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>1.8</td>
<td>2.9</td>
<td>&lt;15%</td>
<td>Yes</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.4</td>
<td>1.7</td>
<td>&lt;15%</td>
<td>No</td>
</tr>
<tr>
<td>Lipids</td>
<td></td>
<td></td>
<td>15-40%</td>
<td>Yes</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.7</td>
<td></td>
<td>&lt;15%</td>
<td>No</td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>TIA</td>
<td></td>
<td>3.9</td>
<td>&lt;15%</td>
<td>Yes</td>
</tr>
<tr>
<td>Carotid Stenosis</td>
<td></td>
<td></td>
<td>&lt;15%</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Gorelick PB, Arch Neurol 1995;52:347
### Population Attributable Risk

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Estimated Percentage Exposed</th>
<th>Estimated Relative Risk</th>
<th>Estimated Population Attributable Risk</th>
<th>Projected number of Stroke Prevented</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>56</td>
<td>2.7</td>
<td>49</td>
<td>246,500</td>
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<tr>
<td>Smoking</td>
<td>27</td>
<td>1.5</td>
<td>12</td>
<td>61,500</td>
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<tr>
<td>Atrial Fib</td>
<td>4</td>
<td>3.6</td>
<td>9</td>
<td>47,000</td>
</tr>
<tr>
<td>Alcohol</td>
<td>7</td>
<td>1.7</td>
<td>5</td>
<td>23,500</td>
</tr>
</tbody>
</table>

Gorelick PB, Stroke 1994;25:220
WASID study
Randomized 69 patients with symptomatic intracranial atherosclerosis
- warfarin sodium INR 2-3
- ASA 1300 mg
Primary endpoint: ischemic stroke, death from vascular cause

**Figure 2. Cumulative Incidence According to Treatment Assignment**

The primary end point was ischemic stroke or death from vascular causes other than stroke.

**Figure 3. The Product-Limit Estimate of the Cumulative Probability of Death (Panel A) and the Cumulative Incidence of Major Hemorrhage (Panel B) after Randomization, According to Treatment Assignment.**
### Table 3. Adverse Events.

<table>
<thead>
<tr>
<th>Event</th>
<th>Aspirin (N=280, 504.4 Patient-yr)</th>
<th>Warfarin (N=289, 541.7 Patient-yr)</th>
<th>Hazard Ratio (95% CI) ( ^\circ )</th>
<th>P Value ( ^\dagger )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with an Event no. (%)</td>
<td>Events per 100 Patient-yr</td>
<td>Patients with an Event no. (%)</td>
<td>Events per 100 Patient-yr</td>
</tr>
<tr>
<td>Death</td>
<td>12 (4.3)</td>
<td>2.4</td>
<td>28 (9.7)</td>
<td>5.2</td>
</tr>
<tr>
<td>Death from vascular causes</td>
<td>9 (3.2)</td>
<td>1.8</td>
<td>17 (5.9)</td>
<td>3.1</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain hemorrhage</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other hemorrhage</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sudden death</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic aneurysm</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death from nonvascular causes</td>
<td>3 (1.1)</td>
<td>0.6</td>
<td>11 (3.8)</td>
<td>2.0</td>
</tr>
<tr>
<td>Cancer</td>
<td>3</td>
<td></td>
<td></td>
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<tr>
<td>Congestive heart failure</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>0</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major hemorrhage</td>
<td>9 (3.2)</td>
<td>1.8</td>
<td>24 (8.3)</td>
<td>5.0</td>
</tr>
<tr>
<td>Brain hemorrhage</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subdural hematoma</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal hemorrhage</td>
<td>6</td>
<td></td>
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<tr>
<td>Ocular hemorrhage</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Genitourinary hemorrhage</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic aneurysm</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>7 (2.5)</td>
<td>1.6</td>
<td>12 (4.2)</td>
<td>2.2</td>
</tr>
<tr>
<td>Fatal</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonfatal</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Einhaupel K et al

Randomized 20 patients with sinus thrombosis

- IV heparin
- placebo

Primary endpoint: clinical outcome at 3 months

Lancet 1991;338:597

20 patients

10 patients

8 complete recovery
2 residual deficits

10 patients

1 complete recovery
6 residual deficits
3 dead
Einhaupel K et al

Retrospective review of outcome in 40 patients with sinus thrombosis and ICH

47 patients with ICH

27 heparin
- 14 complete recovery
- 9 residual deficits
- 4 dead

13 no heparin
- 3 complete recovery
- 1 residual deficits
- 9 dead

Lancet 1991;338:597
LMWH and SST

Prospective, randomized 60 patients
• 3 weeks nadroparin, 3 months oral anticoagulation
• 3 weeks placebo, no warfarin

Primary outcome: clinical at 12 weeks

Figure 2. Percentages of patients with different outcomes after 3 weeks (BI) and 12 weeks (OHS) or death. Vertical: number of patients (rescaled to percentages). Numbers within bars refer to scores on BI (left) and OHS (right). Most patients were fully independent after 3 weeks (BI score 20), but after 12 weeks only a minority were reported to have no symptoms (OHS grade 0).
### Table 2. Length of Follow-up and Number of Primary Events.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (N=130)</th>
<th>Transfusion (N=63)</th>
<th>Standard Care (N=67)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up (mo)</td>
<td>2550</td>
<td>1321</td>
<td>1229</td>
</tr>
<tr>
<td>Total</td>
<td>21.1</td>
<td>22.2</td>
<td>18.3</td>
</tr>
<tr>
<td>Median</td>
<td>19.6±6.5</td>
<td>21.0±5.7</td>
<td>18.3±7.0</td>
</tr>
<tr>
<td>No. of strokes</td>
<td>12</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>11</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Intracerebral hematoma</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Adams, NEJM 1998: 339;5-11
The image shows a Kaplan-Meier survival curve comparing the probability of remaining stroke-free over months between two groups: Transfusion and Standard care. The curve for Transfusion starts higher and remains consistently higher than the Standard care group throughout the observation period of 30 months. The statistical significance is indicated as P=0.002.
- Vasculitis
- PFO and stroke
- Aortic arch disease
- Cryptogenic stroke
- Antiphospholipid syndrome
- Lupus
Ischemic?

Consider Thrombolysis Thrombectomy

Consider Hemicraniectomy

Atrial Fibrillation, Mechanical Valve, Mural Thrombus?

Carotid Atherosclerosis?

Small Vessel?

Intracranial Atherosclerosis?

Sinus Thrombosis, Dissection?

Sickle Cell Disease

Other

Warfarin, or aspirin if contraindicated

CEA or Stent

Risk Factor Modification:
- Antithrombotic
- Statin
- ACE Inhibitor

Anticoagulation

Transfusion, Bone Marrow Tx

Treat specific cause, consultation

Risk Factor Modification:

Consider Thrombolysis Thrombectomy

Consider Hemicraniectomy

Atrial Fibrillation, Mechanical Valve, Mural Thrombus?

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