**A Systematic Review of Immediate Anticoagulation for Ischemic Stroke of Presumed Cardioembolic Origin**

To the Editor:

In the meta-analysis of randomized controlled trials on the efficacy and safety of anticoagulant treatment in acute cardioembolic stroke, the timing of anticoagulation in these patients is still a controversial issue. Thus a critical review of all published literature is essential to generate consensus and also as a starting point for further research.

We also performed, presented (ENS Meeting 2006) and published as an abstract a systematic review and meta-analysis on this subject that was not mentioned in Paciaroni’s et al review, probably because when our review was presented, his paper was already submitted. Our results also did not support the routine use of anticoagulants in the first 48 hours of an ischemic stroke of presumed cardioembolic origin.

We now update the review including 8 studies: CESG, IST, Fiss bis, TOAST, HAEST, TAIST, Camerlingo et al and ARGIS-1 (LaMonte, unpublished data, 2006). The ARGIS-1 study was not included in Paciaroni’s et al review.

Results reveal a significant increase in symptomatic and asymptomatic hemorrhages when comparing anticoagulation with no anticoagulation or aspirin (Figure 1), but favor treatment with anticoagulants for the prevention of recurrent ischemic stroke or stroke of unknown cause (Figure 2).

As we included ARGIS-1 in the review, we could additionally conclude for the lack of evidence in favor of anticoagulants relatively to a favorable outcome at 3 months (Figure 3).

The review of the methodology of individual studies disclosed several important bias and quality limitations. Only one trial was specifically designed for cardioembolic strokes. This trial supported acute anticoagulation in nonhypertensive patients, but it was prematurely terminated. All other trials excluded patients with clear indications for anticoagulation. CT scan before treatment was not required for patient inclusion in IST. Low weight was temporarily an exclusion factor in TOAST trial. Advanced age and stroke severity were also exclusion factors in several trials.

Taking into account these methodological limitations, we think that a new pragmatic randomized clinical trial is needed.

**Disclosures**

None.


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### Table: Comparison between anticoagulation and no anticoagulation for the presence of symptomatic and asymptomatic cerebral hemorrhages.

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (fixed) 95% CI</th>
<th>Weight</th>
<th>OR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CESG</td>
<td>0/24</td>
<td>2/21</td>
<td>6.50 (0.16, 3.51)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Camerlingo</td>
<td>10/93</td>
<td>2/85</td>
<td>4.65 (1.06, 23.52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAEST</td>
<td>24/224</td>
<td>32/235</td>
<td>7.97 (0.46, 1.38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IST</td>
<td>32/1557</td>
<td>7/1612</td>
<td>16.60 (2.12, 10.93)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAIST</td>
<td>7/256</td>
<td>0/112</td>
<td>1.66 (0.38, 11.45)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>2154</strong></td>
<td><strong>2055</strong></td>
<td><strong>100.00 (1.17, 2.54)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 18.53, df = 4 (P = 0.0010), I² = 78.4%

Test for overall effect: Z = 2.73 (P = 0.006)

Figure 1. Comparison between anticoagulation and no anticoagulation for the presence of symptomatic and asymptomatic cerebral hemorrhages.

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Figure 2. Comparison between anticoagulation and no anticoagulation for the recurrence of stroke (ischemic or unknown cause).

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (fixed) 95% CI</th>
<th>Weight %</th>
<th>OR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CECG</td>
<td>9/24</td>
<td>2/31</td>
<td>2.63 (0.16, 3.51)</td>
<td>15.68</td>
<td>1.13 (0.57, 2.24)</td>
</tr>
<tr>
<td>HAEST</td>
<td>19/226</td>
<td>17/225</td>
<td>76.21 (0.39, 0.82)</td>
<td>2.77</td>
<td>0.87 (0.16, 4.84)</td>
</tr>
<tr>
<td>IST</td>
<td>44/1557</td>
<td>79/1612</td>
<td>2.70 (0.17, 3.56)</td>
<td>2.77</td>
<td>0.87 (0.16, 4.84)</td>
</tr>
<tr>
<td>TAIST</td>
<td>4/256</td>
<td>2/112</td>
<td>100.00 (0.47, 0.88)</td>
<td>2.77</td>
<td>0.87 (0.16, 4.84)</td>
</tr>
<tr>
<td>TOAST</td>
<td>0/143</td>
<td>2/123</td>
<td>100.00 (0.47, 0.88)</td>
<td>2.77</td>
<td>0.87 (0.16, 4.84)</td>
</tr>
</tbody>
</table>

Total (95% CI): 2204 / 2093

Test for heterogeneity: Chi² = 4.77, df = 4 (P = 0.31), I² = 16.1%
Test for overall effect: Z = 2.77 (P = 0.006)

Figure 3. Comparison between anticoagulation and no anticoagulation for the presence of favorable outcome at 3 months.

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (fixed) 95% CI</th>
<th>Weight %</th>
<th>OR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARGIS-1</td>
<td>7/11</td>
<td>3/6</td>
<td>4.58 (1.75, 13.16)</td>
<td>95.42</td>
<td>0.94 (0.56, 1.58)</td>
</tr>
<tr>
<td>TOAST</td>
<td>97/143</td>
<td>85/123</td>
<td>100.00 (0.59, 1.62)</td>
<td>95.42</td>
<td>0.94 (0.56, 1.58)</td>
</tr>
</tbody>
</table>

Total (95% CI): 154 / 129

Test for heterogeneity: Chi² = 0.34, df = 1 (P = 0.56), I² = 0%
Test for overall effect: Z = 0.08 (P = 0.94)
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