Updates in Neurointervention

Amit N. Sanghvi MD
Honolulu, Hawaii — Results of the Interventional Management of Stroke III (IMS-III) trial show no benefit of endovascular therapy after the use of intravenous (IV) thrombolysis over IV thrombolysis alone in the treatment of moderate to severe acute ischemic stroke.

Full results were presented here today at the International Stroke Conference (ISC) 2013 by principal investigator Joseph P. Broderick, MD, from the University of Cincinnati, Ohio, at a session dedicated just to this trial. Results were published online simultaneously in the New England Journal of Medicine.

"Overall, the combination therapy as compared to standard IV tPA [tissue plasminogen activator], there was no difference in safety," Dr. Broderick told Medscape Medical News, including hemorrhage rates and mortality. "But we didn’t see a signal of efficacy, better functional outcomes," he said, with no statistical difference seen in the primary efficacy outcome between the groups.

There was some suggestion that patients with more severe strokes and strokes in the larger arteries may benefit from endovascular therapy, particularly if it can be provided rapidly.
SAN FRANCISCO — Microsurgical clip occlusion does not prevent disabilities any better than endovascular coil embolization in most patients with subarachnoid hemorrhage stemming from cerebral aneurysms, a new study shows.

But coiling does a better job of obliterating the aneurysms and requires less retreatment, the researchers said.

"A strong case can be made that anterior circulation aneurysms should be clipped," said first author Robert Spetzler, MD, director of the Barrow Neurological Institute in Phoenix, Arizona. "Picking which patients for which treatments remains an art, unfortunately not based on science."

Dr. Spetzler presented 6-year results of the Barrow Ruptured Aneurysm Trial (BRAT) here at the American Association of Neurological Surgeons (AANS) 82nd Annual Meeting.

Head-to-Head Trial

With similar outcomes for the 2 procedures reported in previous trials, Dr. Spetzler and his colleagues set out to compare the 2 treatments head-to-head. They randomly assigned 238 patients with ruptured aneurysms to clipping and 232 to coiling.

Six years later, 336 patients who had received treatment were available for evaluation. Thirty-eight percent of patients assigned to coiling crossed over to clipping, and 2% of the clipping patients crossed over to coiling.

At the end of the first year, the 24% of the coil-assigned patients had modified Rankin Scale (mRS) scores greater than 2, indicating mild to severe disability. In contrast, 35% of the clip-assigned patients had mRS scores that high. The difference was statistically significant ($P = .03$).

But by the third year, results published in the Journal of Neurosurgery in 2013, showed that the difference had disappeared, and although there was a 5.8% absolute difference with coiling vs clipping, the difference was not significant.

And at the sixth year, the most current results reported here, the score stood at 35% for coiling vs 41% for clipping, a difference that was not statistically significant ($P = .24$).

"We've got to remember that aneurysm treatment has to last a lifetime, not just a few years," said Dr. Spetzler.
Updates in Neurointervention

- IMS III trial:
  - What does this mean for daily stroke intervention?
  - Is stroke intervention safe?
  - Should we provide this care?
Barrow Ruptured Aneurysm Trial (BRAT)

- Should we clip more aneurysms?
- Should coiling brain aneurysms be considered a first line therapy?
- ISAT results vs BRAT trail
Phase 3, randomized, open-label international trial comparing a combined intravenous and intraarterial stroke treatment vs intravenous tPA alone.

Trial was halted in April 2012 when a preplanned interim analysis showed "a low likelihood of demonstrating the pre-specified clinically significant difference in benefit between treatment arms of the study"
The trial showed similar safety outcomes and no significant difference in functional independence with endovascular therapy after intravenous t-PA, as compared with intravenous t-PA alone.
Our Best Sites is Too Long

- Onset to Arrival: 57 minutes
- Arrival to IV: 66 minutes
- IV to Groin Puncture: 86 minutes
- Groin to IA Treatment: 44 minutes

Minutes: 0 50 100 150 200 250 300
Time to IV t-PA and Time from t-PA to Groin Puncture

<table>
<thead>
<tr>
<th>IV tPA to Puncture</th>
<th>Onset to IV</th>
<th>1.5</th>
<th>1.50</th>
<th>0.98</th>
<th>1.32</th>
<th>1.29</th>
<th>1.86</th>
<th>1.17</th>
<th>1.80</th>
<th>0.97</th>
<th>1.44</th>
<th>0.80</th>
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<td>All IV t-PA Treated (N=222)</td>
<td>1.15</td>
<td>[0.88, 1.50]</td>
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<td>&gt;90 Minutes (N=177):</td>
<td>All IV t-PA Treated (N=222)</td>
<td>0.98</td>
<td>[0.72, 1.32]</td>
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<td>[0.90, 1.86]</td>
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<td>&gt;90 Minutes (N=90):</td>
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<td>1.17</td>
<td>[0.76, 1.80]</td>
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<td>&lt;=90 Minutes (N=111):</td>
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<td>[0.66, 1.44]</td>
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<tr>
<td>&gt;90 Minutes (N=87):</td>
<td>&gt;120 Minutes (N=103)</td>
<td>0.80</td>
<td>[0.52, 1.25]</td>
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Commentary from Neurosurgery

- (1) the absence of competing therapeutic alternatives for non-IV rtPA eligible patients
- (2) the importance of pre-procedural arterial imaging to identify and distinguish strokes due to Large-Vessel Occlusions (LVO)
- (3) the advantage of endovascular therapy in patients with confirmed LVO by pre-procedural imaging
- (4) dramatic improvements in the technical performance and safety profile of modern endovascular devices.
Translation to “Real Life”

- 1. Give IV tPA ASAP
- 2. Identify patients with possible LVOs
- 3. Obtain rapid imaging in possible LVOs
- 4. Treat with intervention ASAP !!!!!

Then vs Now
- 7 years ago devices were a “stone hammer”
- Current – Advanced Safe Devices.
Case 1

- 68 year old with occasional right arm tingling and weakness.
Case 2

- 45 year old male who presents at outside facility at ~20:30 pm. 1 hour after symptoms.
- NIHSS 13. Left sided paralysis and global decrease in LOC
- Flown from Winamac (Pulaski) to Fort Wayne. Met helicopter on arrival
- Treatment started at ~2400
Case 3

- 80 year old patient with atrial fibrillation.
- NIHSS ~10. Left sided weakness, facial asymmetric, transitory loss speech.
- No tPA due to coumadin tx and elevated INR.
- Direct transfer from outside site to IR.
Barrow Ruptured Aneurysm Trial (BRAT)

- 500 eligible patients who were enrolled prospectively in the study
- 238 patients were assigned to aneurysm clipping
- 233 to coil embolization
1 Year

- Poor Outcome (mRS score > 2) was observed in
  - 33.7% aneurysm clipping
  - 23.2% coil embolization (No rebleed)

- No debate on posterior circulation aneurysms.
Barrow Ruptured Aneurysm Trial

3 Year
- 3 years' follow-up 349 patients who had actually undergone treatment were available for evaluation
- Risk of a poor outcome (anterior circulation):
  - Clipping 35.8% vs Coiling 30% (Not Statistically Significant)

6 Year
- Risk of a poor outcome (anterior circulation):
  - Clipping 41% vs Coiling 35% (Not Statistically Significant)
  - 4% of the clipped patients needed retreatments vs 13% of the coiled patients, a difference that was statistically significant (P = .001).
A strong case can be made that anterior circulation aneurysms should be clipped," said first author Robert Spetzler, MD, director of the Barrow Neurological Institute in Phoenix, Arizona. "Picking which patients for which treatments remains an art, unfortunately not based on science."
"This is a really terrific trial," said Robert Rosenwasser, chair of neurosurgery at Thomas Jefferson University in Philadelphia, Pennsylvania, in official comments on the study as part of the AANS session.

He pointed out that surgeons at his institution have gotten better results with coiling than clipping in some categories of patients, especially those with posterior circulation aneurysms and those with poor-grade aneurysms and in patients with major medical morbidities.

"I think each institution needs to look at their own morbidity and mortality. Not everyone can go to Phoenix; not everyone has the skill set that the Barrow group has. And I think that there may be instances where endovascular therapy may have a better outcome at your own institution."
Clip vs Coil

Clipping Treatment for Cerebral Aneurysm

Coil Procedure for Cerebral Aneurysm
43 year old with headache and LOC.
Case 2

- 34 year presents with headache for past few months. Blurry vision.
Case 3

- 60 year old with difficulty to breath.
Conclusion 1

- IV tPA remains the first line treatment in acute stroke.
- Endovascular treatment in acute stroke should be limited for patients with LVO, inability to receive tPA and as a recuse therapy option.
- Endovascular therapy is safe.
- Additional trails are ongoing to continue to evaluate new devices.
Endovascular treatment of brain aneurysms remains first line therapy.

Though the information is present in the BRAT would suggest there is equivocal results at 3/6 years, results need to be correlated at local sites.