The Barrow Ruptured Aneurysm Trial

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Prior to this trial, the ISAT trial (2002) demonstrated better outcomes in patients treated with endovascular coiling vs. surgical clipping following a ruptured intracranial aneurysm. However, there were several limitations to this study, namely the selective pre-screening criteria for enrollment (of 9559 aneurysms screened, only 2143 were enrolled) and questions regarding the clinical proficiency of the treating physicians. For this reason, the BRAT study was designed to address some of these limitations inherent to the ISAT trial, with the goal of further defining the role of open vs. endovascular techniques for intracranial aneurysms, and perhaps determining if one technique was superior to the other in terms of both clinical and angiographic outcomes.

Experimental design and statistics: This was a prospective, randomized controlled trial, enrolling patients with acute, ruptured intracranial aneurysms. Inclusion criteria included age 18-80 yrs and an admission for an acute, non-traumatic SAH, including those with an unclear SAH etiology/cause. Exclusion criteria included a (+) traumatic SAH and a presentation >14d following their hemorrhage. Following enrollment, patients were randomized (1:1) to receive either open or endovascular therapy, ideally within 24hrs of admission. Two surgeons participated in each mode of treatment, and patients were made aware of both treatment modalities.[1] Patients were also able to cross over the alternate treatment approach during the study, if appropriate. Following admission, all enrolled patients obtained the same protocol of pre/post-op care (including vasospasm mgmt), and all underwent cerebral or CT angiography before surgical intervention. Prior to intervention, treating neurosurgeons reviewed imaging studies to determine the appropriateness of each patient's assigned treatment modality. Cross over could occur here if the treating physician felt that the alternate approach was a better option.[2] The primary outcome was the proportion of patients with an mRS of 3-6 at 1yr (poor outcome), assessed in an intention-to-treat fashion. Secondary analyses included outcomes related to each patient's actual treatment (i.e., accounting for cross-over), rather than via the intent-to-treat protocal. Re-treatment and re-bleed events were also analyzed. Wilcoxon rank-sum tests, Chi-square tests, and logistic regression methods were used to analyze primary and secondary outcomes.

Results: Following initial screening and consent, 472 patients were eligible for analysis, with 238 assigned to clipping and 233 to coiling; a total of 408 patients obtained actual treatment. Untreated patients were those who either died pre-treatment or who had no SAH/aneurysm found on imaging. Baseline patient characteristics were similar among the two treatment groups (**Table 1**), and cross over to the alternate treatment occurred in 4 patients from the assigned-clipping and in 75 from the assigned-coiling group[3]. In terms of the primary outcome (intent-to-treat analysis), an mRS of 3-6 at 1yr occurred in 33.7% of the clipping group vs. 23.2% of the coiling group (OR of poor outcome: 1.68, p = 0.02; **Table 3**). After adjusting for confounders (age > 50, HH score > II on admission), patients in the clipping group were still 72% more likely to have a poor outcome at 1yr vs. the coiling group. Results were similar (33.9% poor outcome with clipping, 20.4% poor outcome with coiling; OR: 2.28, p = 0.005) when data were analyzed via each patient's actual treatment (i.e. data from patients initially assigned to AND who crossed over into each treatment mode) and when analyses excluded all patients who crossed

[1] All surgeons had a minimum of 3yrs of independent practice and experience with >50 aneurysms

[2] Cross over could also occur if an attempted treatment modality failed

[3] Cross over to the clipping group occurred primarily when anatomical features of an aneurysm inherently favored clipping; SAH grade or patient clinical condition did not play a role in this decision

over in any direction. In the patients who did cross over, a poor outcome was seen in 33.9% who crossed over to clipping from coiling vs. 75% who crossed over to coiling from clipping, with no significant differences here. Otherwise, in terms of retreatment outcomes at 1yr (via intent to treat), 7 (2.94%) events occurred in the assigned-clipping group vs. 16 (6.9%) in the assigned-coiling group (OR: 2.44, $p = 0.05$, **Table 6**). Results were similar when analyzed based on actual treatment (2.34% in clipping vs. 10.62% in coiling; OR: 2.57, $p = 0.03$).

Conclusions: Overall, data from this study expanded that from the earlier ISAT trial by demonstrating fewer poor outcomes, at least at 1yr, following coil embolization vs. surgical clipping for ruptured intracranial aneurysms in a broad SAH population. As the direction of results and magnitude of group differences were sustained regardless of how the data were analyzed (intent to treat vs. actual treatment), the authors note that any poor outcomes were attributed to a patient's originally assigned treatment rather than due to the cross-over design. Importantly, however, endovascular coiling did lead to higher rates of later re-treatment as compared to clipping, suggesting that these patients require close follow up post-procedure. Notably, data from this study reflected only the 1yr follow up data, and later follow up analyses (3 and 6yr) showed no clear differences in outcomes between the two treatment modalities, though this seems to depend upon aneurysm location (anterior vs. posterior circulation). Later follow up analyses still showed higher re-treatment rates in the coiling vs. clipping groups. As such, the authors from this and subsequent follow up analyses have advocated for consideration of either treatment option relative to an individual patient context, when appropriate.

Additional reading, if interested:

1) Speltzer, R.F et.al., The Barrow Ruptured Aneurysm Trial: 3-year results. J Neurosurg (2013). 119: 146-157.
2) Speltzer, R.F et.al., The Barrow Ruptured Aneurysm Trial: 6-year results. J Neurosurg (2015). 123: 609-617.

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