ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations)

This study has been completed.

Sponsor: Columbia University

Collaborator: National Institute of Neurological Disorders and Stroke (NINDS)

Information provided by (Responsible Party): Jay Preston Mohr, Columbia University

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The highly controversial ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations) study marked an important turning point in the history of the management of unruptured cerebral arteriovenous malformations (AVMs).

The ARUBA trial is often subject to polarized interpretation based on extreme views and unflattering logic. It should be viewed in light of its values, the first randomized trial of Unruptured Brain Arteriovenous Malformations, but its conclusion should also be interpreted in light of its methodologic limitations. It has had an impact on bAVM referral patterns.

ARUBA will remain a landmark trial and will likely influence bAVM research for decades to come. Certain clinical practice recommendations may also be deduced from ARUBA, but these do not stem from the analysis of the primary outcome. Clinical decision-making illustrated in the trial should be avoided, as it leads to disastrous results and low obliteration rates, even for Spetzler-Martin AVM grading system grades I and II bAVMs.

The ARUBA trial showed that medical management alone is superior to medical management with endovascular treatment for the prevention of death or stroke in patients with unruptured brain arteriovenous malformations followed up for 33 months. The trial is continuing its observational phase to establish whether the disparities will persist over an additional 5 years of follow-up [1)].

In a nationally representative sample, Reynolds et al. found no change in rates of interventional unruptured AVM management after publication of the ARUBA trial results [2)].

The management of unruptured brain arteriovenous malformations (ubAVMs) remains controversial despite ARUBA trial.

However, microsurgery occurred in only 14.9% of ARUBA intervention cases, raising concerns about the study's generalizability.

The design and conclusions are controversial, and its structure limits analysis of patients who could potentially benefit from treatment.

Unruptured cerebral arteriovenous malformations (AVMs) in pediatric patients (age <18 years) were excluded from the trial.

While the ideal choice of therapeutic modality remains controversial, a multidisciplinary treatment approach for the management of sAVMs can lead to acceptable neurological outcome [3].

The results of ARUBA-eligible and unruptured grade I/II patients overall show that excellent outcomes can be obtained in this subgroup of patients, especially with surgical management. Functional outcomes for ARUBA-eligible patients were similar to those of patients who were randomized to medical management in ARUBA. On the basis of these data, in appropriately selected patients, Nerva et al. recommend treatment for low-grade BAVMs [4].

The ARUBA study has been the object of comments and editorials.

Magro et al., aim to systematically review critiques, discuss design issues, and propose a framework for future trials.

The authors performed a systematic review of the French and English literature on the ARUBA study published between January 2006 and February 2015. The electronic search, including the Cochrane Library, MEDLINE (PubMed and Ovid), CINAHL, and EMBASE databases, was complemented by hand searching and cross-referencing. The comments were categorized as items related to the design, the conduct, and the analysis and interpretation of the trial.

Thirty-one articles or letters were identified. The pragmatic design, with heterogeneity of patients and lack of standardization of the treatment arm, were frequently stated concerns. The choice of outcome measures was repeatedly criticized. During the trial, low enrollment rates, selection bias, and premature interruption of enrollment were frequent comments. The short follow-up period, the lack of subgroup analyses, the lack of details on the results of the various treatments, and a contentious interpretation of results were noted at the analysis stage. A fundamental problem was the primary hypothesis testing conservative management. The authors believe that other trials are needed. Future trials could be pragmatic, test interventions stratified at the time of randomization, and look for long-term, hard clinical outcomes in a large number of patients.

In the authors' view, the ARUBA trial is a turning point in the history of brain AVM management; future trials should aim at integrating trial methodology and clinical care in the presence of uncertainty [5].

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2)
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3)

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4)

Nerva JD, Mantovani A, Barber J, Kim LJ, Rockhill JK, Hallam DK, Ghodke BV, Sekhar LN. Treatment Outcomes of Unruptured Arteriovenous Malformations With a Subgroup Analysis of ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations)-Eligible Patients. Neurosurgery. 2015 Jan 29. [Epub ahead of print] PubMed PMID: 25635891.

5)

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