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Original Article

The Treatment of Brain Arteriovenous Malformation Study (TOBAS): A preliminary inter- and intra-rater agreement study on patient management

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ABSTRACT

Object. – The best management of brain arteriovenous malformation (bAVM) patients remains unknown. Randomized allocation may be more readily accepted when there is uncertainty and disagreement regarding the management of potential participants. In planning for a trial, we aimed to assess variability and agreement among physicians managing bAVM patients.
Methods. – A portfolio composed of 35 patients was sent to 47 clinicians of various specialties managing bAVM patients. For each patient, physicians were asked their best management decision (surgery/embolization/radiosurgery/conservative), their confidence level, and whether they would include the patient in a randomized trial comparing conservative and curative management. Seven physicians, who had access to all images of each patient, independently responded twice, to assess inter and intra-rater agreement using kappa statistics.
Results. – The inter-rater agreement (30 raters, including 16 neuroradiologists) for best management decision was only "fair" (κ [95%CI] = 0.210[0.157; 0.295]). Agreement remained below 'substantial' (κ < .6) between physicians of the same specialty, and when no distinctions were made between various treatments (when responses were dichotomized as conservative versus curative). With access to all images the inter-rater agreement remained fair. The intra-rater agreement reached "substantial" only for the dichotomized decisions. Responding clinicians were willing to include 54.4% of patients (mainly unruptured bAVMs) in a randomized trial.
Conclusion. – There is a lack of agreement among clinicians involved in the management of bAVM patients. In this study a substantial proportion of clinicians were willing to offer randomized allocation of management options to a substantial number of patients.

Introduction

Cerebral arteriovenous malformations (AVMs) are a group of uncommon, heterogeneous lesions that can lead to significant neurological disability or death, most commonly from intracranial hemorrhage [1–3]. Three different treatment modalities are commonly employed in managing patients (surgical resection; endovascular embolization; radiotherapy) alone or in various combinations, depending on local expertise, size, location of the lesion, and clinical presentation. A recent survey has demonstrated substantial variability in opinions regarding which patient/AVM characteristics are most relevant to treatment decisions [4].

To date, the care of patients with AVMs has been a matter of case-by-case decisions based on opinion, as none of the treatments

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available have been shown beneficial in a randomized trial. The ARUBA trial, which concerns only unruptured AVMs, has recently been published [5]. ARUBA had the merit of introducing randomized trial methodology to address a fundamental question regarding patient management. The trial demonstrated that better short-term clinical outcomes could be obtained in patients with unruptured AVMs that were managed conservatively, rather than those that underwent intervention. ARUBA had many limitations (reviewed in [6]), including a small number of patients, a short follow-up period, and a primary outcome measure favoring conservative management. A frequent complaint was that all treatment modalities were grouped together; it has since been suggested that a number of poor outcomes resulted from endovascular management of lesions that perhaps could have been more effectively and more safely managed surgically [7,8].

The contested ARUBA results have left the community perplexed: Should all interventions be stopped, or should we continue as if the trial had never been done? Neither reaction seems appropriate [9]. Conventional trial methods may be poorly adapted to this disease, but the previous way of treating patients, without evidence of merit, is no better. The way forward is to provide a care research context to offer patients interventions that may promise a good outcome but that have yet to be shown beneficial [10]. The Treatment Of Brain Arteriovenous malformation Study (TOBAS) is a pragmatic study integrated with normal care [2]. The trial has been launched as a pilot study, but is poised to expand to other centers. Because TOBAS represents a novel way to care for AVM patients, there are two outstanding issues that we sought to address in the present work.

The first regards community uncertainty, a common requirement regarding the propriety of randomized allocation of treatment options, which would be a necessary prerequisite for the expansion of TOBAS. The demonstration that a number of individual clinicians would recommend divergent management options to the same patient with the same AVM, would support the notion that in spite of ARUBA, sufficient community uncertainty exists to proceed with additional randomized trials [11]. Thus the first aim of this work was to study the agreement regarding management decisions for AVM patients among various physicians from various backgrounds and expertise.

The second objective of this work was to estimate how often clinicians would offer patients randomized allocation of management options with a 50% chance of conservative management.

Materials and methods

The present report is written in compliance with the Guidelines for Reporting Reliability and Agreement Studies [12]. To enable the participation of multiple readers from various backgrounds, institutions and countries, inter-observer variability was studied using an electronic survey of selected images of cases of patients with brain AVMs. A second study, restricted to clinicians of a single institution that had full access to all information, including angiographic and MRI data on the same patients on the hospital Picture Archiving and Communication System (PACS), was designed to validate the results of the electronic survey and to more closely mimic normal clinical conditions.

Patients

From Donner [13] (where for an expected K_0 of 0.600 with a prevalence of 0.3 and 5 raters, 24 subjects are sufficient for the lower limit of a 95% one-sided confidence limit to be no less than 0.400), we estimated that 24 cases would be necessary to provide meaningful results. The number of cases was increased to 35 to include ruptured AVMs patients (for whom more frequent agreement was expected) and to obtain a spectrum of patients that would resemble a clinical series. The cases were extracted from the database of the Treatment of Brain Arteriovenous malformation Study (TOBAS), a randomized trial and registry evaluating the management of bAVM [2] (clinicaltrials.gov NCT02098252). One author selected the cases to include at least 50% low-grade lesions (Spetzler-Martin I and II) [14], for which we expected decisions for intervention with curative intent to be common. Minutes were reviewed from the multidisciplinary meeting where interventional neuroradiologists and neurosurgeons had reviewed the cases and made a final management plan as part of the inclusion process for patients in TOBAS. One author collected clinical and imaging data on 35 selected patients as well as the decisions proceeding from the multidisciplinary meeting. The characteristics of the patients included in the portfolio are summarized in Table 1.

Table 1
Characteristics of brain AVM patients included in the portfolio.

	All bAVMs ($n = 35$)	Unruptured bAVMs ($n = 21$)	Ruptured bAVMs ($n = 14$)
Female, *n* (%)	21 (60.0)	12 (57.1)	9 (64.3)
Mean age ± SD	43.7 ± 18.5	45.2 ± 16.5	41.4 ± 21.6
Spetzler-Martin Grade I–II, *n* (%)	19 (54.3)	11 (52.4)	8 (57.1)
Spetzler-Martin Grade III–V, *n* (%)	16 (45.7)	10 (47.6)	6 (42.9)

bAVM: brain arteriovenous malformation.

The electronic portfolio was composed of 121 selected images (3 images for 19 patients and 4 for 16 patients). On each page of the electronic survey, at least 2 relevant angiographic and 1 cross-sectional image (brain MRI [33 patients] or CTA [2 patients]) of a single patient were displayed with a brief clinical history. The following clinical data were made available: patient age and gender, clinical symptoms (for example seizures, headache), history of intracranial hemorrhage (recent/acute or distant/resolved), and the AVM grade according to the Spetzler-Martin classification [14]. The multidisciplinary meeting decision was not displayed.

For each of the 35 cases presented, raters were asked to answer 3 questions:

- What is, in your opinion, the best management option for this patient? Raters had to select from:
  - surgery (which could include pre-operative embolization),
  - embolization (which could be completed by radiotherapy or surgery if incomplete),
  - stereotactic radiosurgery,
  - conservative management;
- What is your confidence level in making your choice? (raters had to select between 0% and 100% in 10% increments);
- Would you recruit this particular patient in a trial proposing a 50% chance of curative treatment and a 50% chance of conservative management? (yes/no).

The complete electronic survey is provided online (electronic portfolio).

Raters

The portfolio was sent to 47 clinicians involved in the management of brain AVMs, listed as potential participants in the TOBAS trial (23 neuroradiologists, 17 neurosurgeons, 7 neurologists). Seven additional raters (4 neuroradiologists and 3 neurosurgeons) from the same institution had access to all images of each patient (MRI and DSA) through the Picture Archiving and Communication