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In the article by Baharvahdat et al[1] in this issue entitled, "Endovascular Treatment for Low-Grade (Spetzler-Martin I–II) Brain Arteriovenous Malformations," the authors retrospectively reviewed a prospectively maintained data base of low-grade brain arteriovenous malformations (bAVMs) using endovascular therapy (EVT) as first-line therapy with attempts to cure during an 11-year period (2005–2015). The primary outcome studied was AVM obliteration, and secondary outcomes included disability or death secondary to embolization using the modified Rankin Scale. The authors included in their analysis only those patients in whom EVT was completed. Patients who were lost to follow-up or for whom additional EVT was planned were excluded. The grading of the AVMs was performed by 2 senior operators not involved in the treatment. Onyx (Covidien, Irvine, California) was the embolic most commonly used, but other agents were also used. The embolization was always transarterial, and a CT scan was obtained after all procedures or immediately if there was a perforation. The procedure was stopped if the AVM was obliterated or if there was unacceptable reflux onto the microcatheter. Clinical assessment using the modified Rankin Scale was performed at "the initial and follow-up visits," whose timing was not defined. Obliteration of the bAVM was defined as negative findings on an angiogram at 6 months. Clinical assessments were performed by a "neurologist independent from the operators . . . ." His or her experience level, board certification, or even the number of different doctors involved was not defined. Neurologic deficits were considered transient if they resolved by 1 month. A modified Rankin Scale score of 0–2 was considered a good outcome.

In total, the authors' interventional team, also not defined in terms of number of operators or experience level, evaluated 330 patients. Only 288 were treated by EVT. The fate of the remaining 42 and the reason they did not receive EVT were not explained. Of the 288 patients, 8 were lost to follow-up and 56 had not yet completed their EVT, leaving a total of 224 patients with completed EVTs who formed the basis of this studied cohort. Of these, 60% presented with hemorrhage, with 21% of the total cohort having a poor initial mRS score (almost all of whom presented with bleeds). Complete obliteration was achieved in 92%; more than two-thirds of the obliterations were accomplished with 1 session. Eleven patients had a delayed hemorrhage (timing not specified), of whom 7 had a permanent deficit. Severe ischemic permanent deficits occurred in 5 patients. In total, 32 patients (14%) developed a new deficit, but 20 patients resolved their deficit by 30 days, yielding a total permanent neurologic complication rate of 5%. Eighty percent of patients had a good mRS score at follow-up, with 6% having a worse postprocedural mRS score on follow-up. There was 1 procedure-related death. The authors found no difference between the success of obliteration and the bAVM location. The only risk factor for a poor mRS score in both the univariate and multivariate analyses was a poor presenting mRS score. The authors concluded that EVT is a good alternative for achieving a complete cure of low-grade bAVMs, with a low complication rate.

The authors quote and compare their series with the A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA) study.[2] The comparison and referencing of the ARUBA study is, however, not relevant. The ARUBA study was limited to unruptured lesions, whereas most patients in the current study (60%) presented with hemorrhage. Another inaccuracy of the current article is that the authors stated that the ARUBA study did not include many low-grade lesions. In fact, approximately 56% of the lesions in ARUBA were grade I or II. Another reason for the poor comparison is that the ARUBA study was a prospective, randomized trial with protocols for enrollment and management and strict inclusion and exclusion criteria with clinical and radiographic outcomes adjudicated by an international committee and an intention-to-treat analysis. This study has none of that and, in fact, has most of the downsides of a retrospective analysis. There is no explanation as to why 42 patients evaluated did not get EVT. Were they somehow deemed different in any way? Potential bias may have been introduced.

The current article does not seem to have any protocol for clinical follow-up and simply states that it was performed. Multiple different interventionalists with different experience using different agents seem to have been used. A heterogeneous group of both hemorrhagic and nonhemorrhagic lesions was included, which makes it impossible to tease out whether the mRS score was

related to the initial bleed or some complication from EVT. Onyx embolic was only released in the United States for clinical use in 2005, and the detachable catheters followed after that. Therefore, some experience across time may have been gained by this interventional team, suggesting that a lesion treated by them in 2015 may have benefitted from a different experience and understanding of the embolic agents and catheter technology than one treated in 2005.

Last, by not including the fate of those who failed EVT, the current study excludes any morbidity accrued from further therapy, which downplays the risk of embarking on EVT as a first-line therapy, something that an intention-to-treat analysis would capture. I would also question whether all of these lesions were, in fact, grade I or II. The lesions included 77 (34%) in an eloquent area of the brain. According to the Spetzler-Martin Grading Scale, if any of these had deep drainage, they would automatically be graded at least a III.[3] Furthermore, they had 19 (8%) lesions that were considered "deep." Many of these were in the eloquent brain and drained to the deep venous system. If any of these were, in fact, eloquent and had deep drainage, they too would be at least a grade III. Again, without independent adjudication, we are left to assume that the lesions were graded correctly, but with such high numbers characterized as "deep" and "eloquent," how confident should we be?

Despite these shortcomings, this publication represents one of the largest series in the modern era of bAVMs treated with an EVT intent-to-cure approach. Restricting their treatment to good grade (Spetzler/Martin I–II) makes it unique. Their obliteration rate (92%) is quite impressive and certainly competitive with the other treatment modalities, namely radiosurgery and surgical excision. Their complication rate, while acceptable, needs to be scrutinized a bit and may not be as sanguine as the authors suggest. The modified Rankin Scale is a coarse scale, which measures function, and does not necessarily take into account subtle or even more overt cognitive dysfunction. Twenty patients in this study had new neurologic deficits after treatment, which resolved within 30 days. It is likely that had MR imaging been performed on these patients, some would have shown strokes with possible accompanying neuropsychological deficits that might not be elicited on a routine neurologic examination.

One of the less discussed results of the ARUBA study was that the natural history risk of unruptured bAVMs was significantly less than previously thought.[4] This result had been previously demonstrated, and evidence suggests that some lesions, particularly certain subsets of bAVMs such as small noneloquent-placed lesions without deep venous drainage, may bleed at a yearly rate of $<1\%$.[5,6] Furthermore, when unruptured AVMs bleed, the resultant morbidity has recently been shown to be less than initially thought.[6] As a result, any offered treatment for unruptured bAVMs must carry quite a low risk to beat the natural history risk. Whether the 5% permanent morbidity (or possibly even higher as outlined above) and 0.4% mortality of EVT for low-grade lesions presented here beats the natural history risk and, more important, whether a given patient would elect to take such a risk is not completely clear. A randomized trial would be needed to help shed light on this important issue.

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Note: The authors were given the opportunity to respond and declined.

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