Editorial

Is a single-staged endovascular embolization and microsurgical resection approach preferred to a multi-staged approach for the treatment of brain arteriovenous malformations?

Hailey S. Novis[1], Adrian J. Rodrigues[2], Gracyn J. Campbell[3], Samuel R. Falkson[4]^

[1]Harvard Medical School, Boston, MA, USA; [2]Department of Neurosurgery, Stanford University Medical Center, Stanford, CA, USA; [3]Dartmouth College, Department of Biomedical Engineering at the Thayer School of Engineering, Hanover, NH, USA; [4]Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Correspondence to: Samuel R. Falkson, MD. Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, 55 Fruit Street, Boston, MA 02114, USA. Email: sfalkson@mgh.harvard.edu.

Comment on: Zeng C, Wang M, Song X, *et al.* Multimodal treatments of brain arteriovenous malformations: a comparison of microsurgical timings after endovascular embolization. Ann Transl Med 2022;10:732.

Submitted Jul 02, 2022. Accepted for publication Jul 17, 2022.
doi: 10.21037/atm-22-3395
View this article at: https://dx.doi.org/10.21037/atm-22-3395

We read with great interest the recent published study by Zeng *et al.* entitled "*Multimodal treatments of brain arteriovenous malformations*: *a comparison of microsurgical timings after endovascular embolization*". This study suggests that a single-staged "*hybrid operation*" that features endovascular embolization and subsequent microsurgical resection during the same anesthetic event to treat brain arteriovenous malformations (bAVMs) may produce similar long-term outcomes compared to a staged approach, with some potential benefits. We appreciate the work of Zeng and colleagues for their valuable study, and would like to add this editorial to further contextualize their findings and offer thoughts for future work on this topic.

Arteriovenous malformations are abnormal connections between arteries and veins without a true intervening capillary bed that produce a pathway for high flow arterial blood to shunt into lower pressure veins. Given the high pressure gradient and subsequent high pressures in the venous system, rupture of bAVMs can lead to the feared complication of intracranial hemorrhage (ICH), a form of hemorrhagic stroke. ICH is one of the leading causes of brain hemorrhage in children and young adults with a prevalence of 10 per 100,000 (1,2). Patients with ICH often present with seizures, headaches, or focal neurologic deficits and have a mortality between 12–67%, depending on clinical sequelae (1). Diagnosis of bAVMs occurs though imaging, either during evaluation of patients presenting with symptoms, or as an incidental finding. Digital subtraction angiography (DSA) provides the definitive diagnosis for bAVMs, as its high degree of temporal and spatial resolution enables accurate and detailed characterization of such lesions (3). Other modalities, including magnetic resonance imaging and computed tomography, can also be used for identification of bAVMs, and can be important for treatment planning (3). There is currently no primary medical therapy available to obliterate bAVMs; treatment involves microsurgical resection, stereotactic radiosurgery, or endovascular embolization.

Selection of the appropriate treatment modality depends upon the specific clinical context and the characteristics of the bAVM. Microsurgical resection of bAVMs can be performed both with and without prior endovascular embolization (4). Endovascular embolization was introduced as a technique to be performed prior to microsurgical resection in an attempt to modify hemodynamic flow through the bAVM to facilitate a safer resection, and to convert inoperable bAVMs to ones suitable for surgical

^ ORCID: 0000-0001-8195-935X.

intervention (5,6). Prior work has shown utility in certain circumstances using this hybrid technique of embolization and resection; yet the optimal time interval between these steps has not been rigorously established (6). Studies over the last 10 years have demonstrated success with combining embolization and resection in a single procedure, though no single study prior to that of Zeng *et al.* has compared outcomes between a single-staged and multi-staged approach (4,6-9). Zeng *et al.*'s work takes a first step towards investigating this comparison in a retrospective case-controlled study, providing data that may suggest certain benefits to a single-staged hybrid approach in the appropriate context.

Zeng and colleagues retrospectively identified and matched bAVM patients who underwent either a single-staged hybrid operation (referred to as the "HO" group) featuring surgical resection immediately after embolization, or a multi-staged operation (referred to as the "MO" group), where resection followed embolization by an interval ranging from days to months. There were 66 matched cases in each group, with baseline demographics and clinical characteristics reportedly similar between groups. Zeng *et al.* report a rupture risk of 4.1% per year for the MO group and no ruptures in the HO group in the time between embolization and resection. Duration of surgical resection was reduced in the HO group. The HO group was less likely to have short-term neurological deficits (ND); yet there were no differences in long-term outcomes between groups. Overall, the authors suggest that the HO modality may be a viable approach to treating bAVMs. While valuable, there are important limitations to this study.

First, we would like to comment on the study design where patients were retrospectively selected through a multi-center approach. While the multi-center approach is important in comparing outcomes across institutions and increasing the generalizability of their findings, it also introduces a potential source of confounding as patients at each institution may be more or less likely to receive the MO or HO strategy based on factors specific to the individual institutions, and not necessarily their clinical scenario. Given the retrospective design, there is no unifying protocol that each institution followed *a priori* to determine treatment modality. Indeed, Zeng *et al.* specifically state that the management approach was in part dependent on the individual neurosurgeons in the different medical centers. Given the relatively small number of patients in this study, differences in outcomes may be due to differences in the clinician performing the procedure or their supporting clinical environment and resources, as opposed to the therapeutic approach. Such concerns would be best addressed in prospectively-conducted randomized controlled trials.

We would also like to discuss patient matching in the study. As explained in Zeng *et al.*'s study, HO and MO groups were matched according to the characteristics of their bAVMs defined through the field-standard Spetzler-Martin grading scale. While baseline demographics reportedly showed no difference, it is important to note that a propensity score matching (PSM) analysis would have reportedly lowered the number of subjects substantially, suggesting the possibility that patients in the HO and MO group may in fact have had notable differences. Additionally, potentially important variables, including level of physician experience and hospital volume, do not appear to be included in the matching schema. Given this study's observational nature, limitations in MO and HO group matching make it more difficult to ascertain the effect of the compared treatment modalities versus that of possible confounders.

In future studies, we believe further attention to the anatomical location of the bAVMs would be valuable additional data to describe, as bAVM outcomes are known to vary based on such factors. For example, posterior fossa bAVMs portend a poorer prognosis with higher risk of rupture compared to supratentorial bAVMs (1,10,11). These varying outcomes by bAVM location or characteristics follow logically by considering the functions of the brain structures surrounding the bAVM, and thus most susceptible to injury following rupture. Zeng *et al.* do report bAVM location as either supratentorial or infratentorial, though more granular anatomical description may offer further insight into optimal treatment strategies in particular cases. Future research including additional description of bAVMs (for example by specific location, size, morphology, and patient characteristics) might elucidate that certain bAVMs are more or less suitable to a staged versus single setting approach of embolization and resection.

Lastly, we think further investigation into the time interval between embolization and microsurgery in the MO group could yield valuable results, as the time interval in this study was highly variable, ranging from days to months. This large range makes us wonder whether there was a trend in patient outcomes associated with shorter or longer intervals between embolization and microsurgery. Additional attention to this time interval may be important,

as the work of Zeng *et al.* suggests that timing of subsequent microsurgery is an essential difference between outcomes in the single-staged versus multi-staged treatment of bAVMs. Future studies may find that the ideal time interval between embolization and resection varies as a function of the characteristics of the bAVM.

In summary, Zeng *et al.* present a retrospective case-control study evaluating outcomes in patients with bAVMs using both a multi-staged approach featuring embolization followed by microsurgery versus a hybrid approach featuring embolization and microsurgery performed in a single setting. Their findings suggest that the hybrid procedure may have short-term benefits, in appropriately selected patients, over a multi-staged procedure, including decreased surgical resection time, interval hemorrhage risk, and likelihood of short-term NDs. The hybrid approach also offers logistical benefits in terms of convenience to patient and provider, and by avoiding the risks of subjecting patients to multiple anesthetic events given that the bAVM can be intervened upon in a single setting. While a larger, prospectively-designed randomized controlled trial would ultimately be a superior modality to compare these two management approaches, the current study provides useful data on this topic. Future work heeding our above discussion regarding study design, patient selection, and further attention to bAVM characteristics will advance our ability to optimally care for patients with bAVMs.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Translational Medicine*. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3395/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Berman MF, Sciacca RR, Pile-Spellman J, et al. The epidemiology of brain arteriovenous malformations. Neurosurgery 2000;47:389-96; discussion 397.
2. Friedlander RM. Clinical practice. Arteriovenous malformations of the brain. N Engl J Med 2007;356:2704-12.
3. Derdeyn CP, Zipfel GJ, Albuquerque FC, et al. Management of Brain Arteriovenous Malformations: A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke 2017;48:e200-24.
4. Chen Y, Li R, Ma L, et al. Single-Stage Combined Embolization and Resection for Spetzler-Martin Grade III/IV/V Arteriovenous Malformations: A Single-Center Experience and Literature Review. Front Neurol 2020;11:570198.
5. Spetzler RF, Martin NA, Carter LP, et al. Surgical management of large AVM's by staged embolization and operative excision. J Neurosurg 1987;67:17-28.
6. Zeng C, Wang M, Song X, et al. Multimodal treatments of brain arteriovenous malformations: a comparison of microsurgical timings after endovascular embolization. Ann Transl Med 2022;10:732.
7. Wang M, Qiu H, Cao Y, et al. One-staged in situ embolization combined with surgical resection for eloquence protection of AVM: technical note. Neurosurg Rev 2019;42:783-90.
8. Murayama Y, Arakawa H, Ishibashi T, et al. Combined surgical and endovascular treatment of complex cerebrovascular diseases in the hybrid operating room. J Neurointerv Surg 2013;5:489-93.
9. Pal S, Nicholson F, Boet R, et al. Multimodality treatment of intracranial arteriovenous malformations in South Island, New Zealand. J Clin Neurosci 2020;73:74-9.
10. Arnaout OM, Gross BA, Eddleman CS, et al. Posterior

fossa arteriovenous malformations. Neurosurg Focus 2009;26:E12.
11. Abla AA, Nelson J, Rutledge WC, et al. The natural history of AVM hemorrhage in the posterior fossa: comparison of hematoma volumes and neurological outcomes in patients with ruptured infra- and supratentorial AVMs. Neurosurg Focus 2014;37:E6.

Cite this article as: Novis HS, Rodrigues AJ, Campbell GJ, Falkson SR. Is a single-staged endovascular embolization and microsurgical resection approach preferred to a multi-staged approach for the treatment of brain arteriovenous malformations? Ann Transl Med 2022;10(14):758. doi: 10.21037/atm-22-3395