In this paper from the respected radiosurgical group at the University of Tokyo, Shin, et al., have provided us with a very good analysis of their experience with gamma knife surgery (GKS) for children and adolescents with cerebral arteriovenous malformations (AVMs). The data are carefully analyzed and the tables provide us with ample detailed information. I do have some concerns about the authors’ interpretation of their data, their use of GKS in this group of patients, and their conclusions. I will express these concerns simply in an effort to balance the paper without detracting in any way from its value.

The authors provide us with a graph to indicate obliteration rates (Fig. 1 in the paper) that is based on “actuarial” rates calculated using Kaplan–Meier life-table analysis. I do not doubt that this is a statistically valid way of presenting the data; however, the strength of results obtained using life-table analysis is dependent on the number of patients at each follow-up point and the numbers in this series are relatively small. For most of us, the results would have been clearer if presented simply as actual obliteration rates based on angiographic findings or on the combination of findings on angiograms and magnetic resonance (MR) images. Because it would be unlikely that every patient in the series would eventually undergo angiography, data of this type could best be presented by giving the “best-case scenario,” which would imply that the AVM was obliterated in every patient who did not undergo angiography, and the “worst-case scenario,” which would assume that a residual patent nidus remained in every patient who did not undergo angiography. Obviously, when data are presented in this way, reality will lie somewhere between best-case and worst-case rates. When we look at the authors’ data in this way, we find an obliteration rate that at best would be 89% (if we assume that the AVM is obliterated in the 18 patients who did not undergo angiography) and at worst would be 71% (if we assume that the AVM remains patent in the 18 patients who did not undergo angiography). Slightly different results can be obtained when the results of the last MR image obtained in patients who did not undergo follow-up angiography are considered. In this case, if we assume that the disappearance of a flow void signal means that the AVM is obliterated, we would obtain a 75% obliteration rate (the 71 patients in whom an obliterated AVM was confirmed by angiography plus the four patients in whom no flow void signal could be found on MR images). Clearly, this last figure of 75% underestimates the eventual obliteration rate given the fact that the follow-up period in some cases is short and we can expect that, in some of these cases, the AVM will eventually be obliterated. The point I wish to make—at least based on my interpretation of the data—is that I do not see much difference between these results and results generally reported on larger series including patients of all ages. In other words, I do not believe that the obliteration rate over the follow-up period in this group of children and adolescents differs significantly from those achieved using radiosurgery for similar AVMs in adults.

It is true that the annual bleeding rate of 1.5% after radiosurgery reported in this series is lower (approximately half) than the average reported in other larger radiosurgical series. Whether this finding is truly related to the generally younger age in this series or whether it is simply a matter of the numbers being relatively small remains speculative. Nevertheless, one patient died, five experienced rebleeding, and four suffered neurological deterioration related to the radiosurgery. As the authors mention, during the microsurgical era, radiosurgical excision of Grade I and II AVMs has been achieved with close to a 0% mortality rate and with serious morbidity rates certainly lower than 5%. In our own experience, we have achieved a combined 0% mortality—serious morbidity rate for a consecutive group of 33 patients with AVMs smaller than 3 cm, who were selected for microsurgical treatment.3 Likewise, we achieved a combined 0% mortality—serious morbidity rate in a consecutive group of 91 patients who underwent surgery for Spetzler–Martin Grade I and II AVMs.2 I admit that this experience includes only a few children, but it does include a significant number of adolescents. Given these results, I believe that the authors’ conclusion that “radiosurgery is an acceptable treatment for arteriovenous malformations: gamma knife surgery

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small AVMs in children and adolescents” should be qualified. Clearly, radiosurgery is an acceptable and, in fact, probably preferable treatment for children, adolescents, and adults with small AVMs located in critical areas of the brain, where a surgical procedure would be likely to result in significant morbidity. Nevertheless, essentially by definition, Grade I and II AVMs do not fall into that category and that is why surgical results for these lesions are so favorable. Therefore, in my opinion, radiosurgery is not an acceptable treatment for “surgically accessible” small AVMs (Spetzler–Martin Grades I and II).

In view of the aforementioned considerations, I am disappointed that, in this particular series, nearly half of the patients (44 of 100) harbored small Grade I or II AVMs. The authors are careful to point out that “for patients harboring a lesion considered to be a good candidate for surgical resection, such as a Spetzler–Martin Grade I or II lesion, we recommend surgical resection as the most reasonable treatment.” They then go on to say, “nevertheless, 44 patients with Spetzler–Martin Grade I or II lesions eventually chose radiosurgery for their treatment.” This reason for including a very large proportion of patients with Grade I and II AVMs is given in many radiosurgical series. I personally have a significant ethical concern about offering a treatment alternative that is less than optimal for a particular patient. We certainly do not do that with other forms of neurosurgical treatment. For example, I hope that we do not offer a patient who harbors a large basal meningioma, which should be treated with an extensive skull-base approach, the alternative of an operation performed through a small “keyhole” craniotomy; such a procedure would achieve better cosmetic results, but would carry greater risk of morbidity and less chance of a cure. Why do we then offer a treatment such as radiosurgery, which is generally admitted to be considerably inferior to surgical excision, to patients with Grade I and II AVMs? I suspect that the majority of patients in this series chose radiosurgery because it was presented as a “reasonable alternative” to microsurgery. I doubt that all 44 patients or their families would have chosen radiosurgery had it been presented as an “inferior” alternative to microsurgical excision. In brief, I feel strongly that it is the physician’s responsibility to present to the patient, in a clear and understandable way, what is “the best” form of treatment for a particular disease. Other less optimal forms of treatment can be discussed, and probably should, but they should be identified as being inferior to the best treatment option when available data clearly indicate which is the best option. Whether to proceed with a less than optimal form of treatment because the patient chooses it remains an open ethical question.

Another important point made by this article is that AVMs in young persons have the potential to bleed even after radiosurgery has achieved complete obliteration, as confirmed by angiography. This, of course, is not unique to radiosurgery and we do know that, in children and adolescents, there is a possibility of redevelopment of an AVM and rebleeding, even after a postoperative angiogram has shown complete obliteration following microsurgical resection. Therefore, it is clear that some form of follow-up imaging is indicated in children and adolescents, even after complete obliteration of the AVM has been confirmed by angiography, regardless of whether the treatment used was radiosurgery or microsurgery.

This article contains important data and the authors are to be congratulated for their very careful follow-up observation of these patients.

References


Response: We appreciate the valuable and thoughtful comments on our paper provided by Dr. Heros. We would like to clarify our standpoint.

No one would disagree that angiography should be the gold standard in evaluating nidus obliteration after radiosurgery; this imaging method most clearly demonstrates the hemodynamic status of an AVM. It would be ideal if all patients could undergo angiography after a sufficiently long follow-up period; however, in reality, there are a certain number of patients who decline angiography, especially when computerized tomography or MR images clearly indicate a residual nidus. Therefore, most clinical studies, including ours, have to deal with a variety of follow-up periods and inhomogeneous data, and statistical methods such as Kaplan–Meier methods are used to minimize this problem while avoiding selection biases. Given that many recent reports of obliteration rates are based on Kaplan–Meier calculations, a comparison of these rates should be performed using numbers calculated in the same manner. Using actual rates only in our analysis would not provide data appropriate for such a comparison. To consider the “best-case scenario” and “worst-case scenario,” as Dr. Heros mentioned, we calculated nidus obliteration in two ways: 1) counting loss of flow void on MR images (four cases) as complete obliteration; and 2) counting this loss of flow void as a residual nidus. Using Kaplan–Meier methods we found that the worst-case scenario still confirms that better nidus obliteration was achieved in the younger patients in our study.

In terms of surgery compared with GKS, we first would like to make it clear that we do not enthusiastically recommend radiosurgery for these younger patients, and we agree with Dr. Heros that microsurgery is the most rational treatment option for small AVMs (< 3 cm in diameter). We explain this fully to all patients, but the decision is ultimately in each patient’s hands. As the first institution to provide GKS in Japan, we receive numerous patients who simply reject the notion of surgery, and such patients may be overrepresented in our series. Some patients have been offered surgery elsewhere, but refused open brain surgery and some had undergone partial resection elsewhere, but would never do it again. We honestly present the patient and family