Perfusion Pressure and Risk of AVM Hemorrhage

TO THE EDITOR: We read with great interest the paper by Spetzler, et al. (Spetzler RF, Hargraves RW, McCormick PW, et al: Relationship of perfusion pressure and size to risk of hemorrhage from arteriovenous malformations. J Neurosurg 76:918-923, June, 1992). The authors describe a direct relationship between relatively elevated "perfusion pressures" within arteriovenous malformation (AVM) feeders and risk of hemorrhage that corresponds to previously cited findings of an inverse relationship between size of an AVM nidus and risk of hemorrhage.

Although we applaud the authors' attempt to define more precisely the pathophysiology of hemorrhagic predisposition of a subpopulation of AVM's, we believe that the methodology and analysis of this study were flawed in several respects. First, we question the validity of identifying and classifying the size of an AVM by cerebral angiography after a hemorrhage has occurred. It is well known (and well documented) that the apparent size of an AVM on angiography will often significantly decrease after hemorrhage. This phenomenon has been attributed to either transient occlusion or permanent obliteration of the nidus from mass effect of the hematoma. We propose that this phenomenon probably introduced significant selection bias into this study (as well as most of the cited references supporting the relationship between "small" AVM's and increased rate of hemorrhage). It is possible that "small" AVM's appear as such because, upon presentation from intraparenchymal hemorrhage, less nidus is usually visualized by angiography. This could lead to a false impression of an association of "small" size and increased rate of hemorrhage. Such a theoretical selection bias is supported by indirect evidence from the current study. For instance, when compared to many other clinical series, there appears to be a disproportionate number of AVM's (almost half) classified as "small." More importantly, the study's finding of an inverse relationship between the size of an AVM and acute hematoma begs for a different interpretation of the data. We suggest that, if it is true that nidus compression/obliteration is produced by mass effect of the hematoma, then a larger hematoma will compress more nidus and result in less visualization of nidus (that is, produce a smaller AVM on angiography). This is precisely what is seen in the data presented in Table 1 of this article.

We believe that the methodology and interpretation of intraoperative pressure measurements in this study were flawed. First, it is erroneous to assume that the intrapedicular pressure measurements made upstream from the edge of an AVM are the same as the "perfusion pressure" of the entire nidus. There is almost certainly a significant pressure drop across the nidus compartment supplied by a given pedicle, which means that in reality the nidus is exposed to a "perfusion pressure gradient." Thus, an isolated upstream pressure measurement provides essentially no useful information about the flow conditions or hemodynamic stresses of a given vascular system, since it is the change in pressure (ΔP) that drives blood flow. Intraoperative measurements of both intrapedicular and intravenous pressure would have been more useful, since this would have provided a better estimate of the net ΔP across the AVM nidus. Furthermore, the simultaneous measurement of either volumetric blood flow or blood-flow velocities would have been invaluable in further defining the flow conditions of a given system. Without these measurements, we are unable to adequately speculate about the etiology of differences in intrapedicular pressures observed in this study. For example, it is difficult to know if the relative elevation of intrapedicular pressures seen with AVM's that bled simply represented "stump" pressures (ΔP = 0) or were due to severe venous outflow obstruction (small ΔP) produced by local mass effect of the hematoma.

In addition, the authors made no attempt to characterize and correlate well-known angiographic factors (such as intranidal or pedicular aneurysms or arteriovenous fistulas) or hemodynamic features (such as restriction of venous outflow, pattern of venous drainage, length of feeder, or vasospasm) obtained from angiography with their intraoperative pressure measurements and clinical presentation. These angiographic features are potentially confounding variables that cannot simply be ignored in the analysis of any possible relationship between intrapedicular pressure measurements and clinical presentation.

Finally, a few of the authors' statements and opinions regarding partial embolization and hemorrhage deserve critical commentary. The authors first state, without references, that there is an increased risk of hemorrhage associated with partial embolization of AVM's. We are not aware of any scientific evidence to support this assertion and have not found this to be true in our own extensive experience with endovascular embolization. On the contrary, there is growing evidence from several embolization/radiosurgery clinical trials that, during the latency period, there is no significant change in the rate of bleeding or rebleeding of partially embolized AVM's. The authors also state, "We have encountered several patients whose AVM's ruptured several days to weeks after transhemorrhage embolization." Without specifying absolute or relative rates. This type of vague, anecdotal statement is unacceptable as the basis of scientific opinion or theory. Most neuroendovascular centers with large case series of brain AVM emboliza-
tion quote an overall postembolization hemorrhage rate of 3% to 5%. In our recent experience of 185 consecutive “partially” embolized AVM’s, nine hemorrhages occurred (4.8%). This hardly constitutes a “frequent” occurrence. Furthermore, the majority of these hemorrhages were attributable to well-established mechanisms, including inadvertent venous outflow obstruction, intradural or pedicular aneurysm rupture, and rupture of a feeding pedicle by a catheter.7

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References


RESPONSE: I appreciate the thoughtful letter by Drs. Chaloupka, Viñuela, and Duckwiler regarding our paper. They raise a number of pertinent points, which deserve comment.

Their first major concern was that a large hematoma could compress a large arteriovenous malformation (AVM) and cause it to appear small. Their reasoning goes that it is logical to be misled in the assumption that angiographically small AVM’s produce larger hematomas. It is interesting that the reference they quote to substantiate their claim is to a chapter by Newton, et al.1 However, in that chapter there are no angiograms that demonstrate the compression or obliteration of an AVM by a hematoma which, after removal of the hematoma, appears angiographically to actually be a giant lesion. In my own personal experience, with well over 250 operations on AVM’s, I have yet to see a giant AVM obliterated by a hematoma to the extent that it angiographically appears like a small AVM unless high intracranial pressure (ICP) has significantly reduced cerebral blood flow. Furthermore, with magnetic resonance imaging, the suspicion that a giant AVM has been compressed or obliterated by a large hematoma should be easily verified. It is particularly true, however, that small AVM’s can be disrupted by hematoma and appear even smaller on angiography. Furthermore, there is no evidence anywhere to suggest that large AVM’s that bleed will appear routinely as small AVM’s on angiography because of the presence of a hematoma. If this observation were true, it would be blatantly obvious to any neurosurgeon operating on these lesions and supported by the many angiograms performed prior to and following the removal of a hematoma associated with an AVM. In contrast, however, is the much more common absence of a true angiographic AVM in association with a large hematoma, while in fact at the time of surgery a small AVM is seen in the wall of the hematoma bed. The initial AVM disruption and associated large hematoma reflects the fact that a true high-pressure arterial bleed has occurred, and this is consistent with our hypothesis. I must therefore respectfully completely reject as an explanation for the discrepancy between AVM size and the size of an associated intracerebral hematoma the suggestion that the size of a hematoma directly determines AVM size.

The next issue raised by Chaloupka, et al., concerns the methodology and interpretation of our intraoperative pressure measurements. They considered these flawed, believing that it is erroneous to assume “the intrapedical pressure measurements, made upstream from the edge of an AVM are the same as the ‘perfusion pressure’ of the entire nidus.” This is naturally completely true and requires no further discussion. That a perfusion gradient is present across the AVM is also a given fact. However, to say that an isolated upstream pressure measurement provides no useful information about the flow conditions or hemodynamic stresses of the given vascular system is completely erroneous. Since the pressure measurements are obtained at the edge of an AVM with the cranium open (with a negative ICP effect) they do indeed provide a very real measurement of the perfusion pressure gradient. The relationship between systemic blood pressure and pressure within the feeding vessels of the AVM is almost a 1:1 ratio. There is no significant change in pressure until the resistance of the AVM is encountered. The measurement obtained at the edges of the AVM nidus is directly related to the resistance and flow of the AVM. We have performed hundreds of AVM pressure measurements, typically including multiple arterial pedicles, the AVM nidus, and the draining veins. Additionally, we have performed computerized tomography-xenon bloodflow studies, 133Xe blood-flow measurements, and Dop-
Doppler ultrasound blood-flow studies on a large cohort of patients. We did not consider that the presentation of these measurements was essential to our discussion. In brief, venous pressure measurements vary a great deal between AVM's, but generally the greatest degree of change (ΔP) occurs in the small AVM's between the feeding arterial pedicle and the venous outflow, as compared to the large AVM's. Again, this is a reflection of the degree of resistance and flow through the AVM.

The authors go on to state that "simultaneous measurement of either volumetric blood flow or blood-flow velocities would have been invaluable in further defining the flow conditions of a given system." If we exclude direct arteriovenous fistulas, there is no question that volumetric flows change dramatically as we progress from small to large AVM's. The crucial questions concern not only how to obtain these volumetric flows and keep them meaningful but also how to determine what pertinent information they could provide that would affect the present hypothesis. The usefulness of blood-flow velocities is very debatable for Doppler ultrasound measurement. Further, they argue that "Without these measurements, we are unable to adequately speculate about the etiology of differences in intrapelvic pressures observed in this study." They have again failed to mention how providing these measurements would help them. Surely, given hundreds of measurements by multiple investigators, there can be absolutely no question that there is a much lower perfusion pressure along the edge of a giant AVM compared with a small AVM. This fact persists regardless of whether there is an associated hematoma.

We were also chastised for not including the characterization of "well-known angioarchitectural...or hemodynamic features" that might relate to hemorrhage. I do not deny the presence and importance of these factors but have difficulty verifying their true contribution to hemorrhage in a particular individual. A problem exists when an attempt is made to pick out retrospectively angiographic variables that contribute to the frequency of bleeding in patients with AVM's who have already bled. Indeed, on review of our own case material, we confirmed that the larger the AVM the greater the likelihood of finding such angiographic variables. This would lead one to think that the risk of hemorrhage should be higher in the large lesions, when it is not so. Venous outflow restriction is surely important, but I have yet to find a case at surgery where the pressure drop is greatest before and after venous constriction as opposed to across the AVM itself. Indeed, for well over 15 years, I have been greatly impressed by the variability of venous drainage and absence of normal venous drainage patterns in patients who harbor AVM's. The very nice paper by my esteemed colleague Fernando Viñuela addressing this topic emphasized that variability. However, a firm relationship between these abnormal venous patterns and a subsequently documented increased risk of bleeding has not been established.

Finally, the authors conclude with a criticism of what appears to be a most sensitive issue: the possibility that an increased risk of hemorrhage occurs with partial embolization of AVM's. They state that "On the contrary, there is growing evidence from several embolization/radiosurgery clinical trials that, during the latency period, there is no significant change in the rate of bleeding or rebleeding of partially embolized AVM's." At first glance at these data, this in fact appears to be the case. However, when examined closely the data demonstrate exactly the opposite finding. I have commented on this issue, first at a meeting in Verona, Italy, and most recently before the Stereotactic Section at the 1992 Congress of Neurological Surgeons' meeting in Washington, D.C. A posttreatment bleeding rate which remains constant during a 2- to 3-year period following focused radiation therapy speaks eloquently to the fact that as these AVM's become smaller they must therefore have an increased tendency to bleed given that the number of AVM's available for bleeding (before complete obliteration) is constantly decreasing. Thus, the constantly decreasing pool of patients whose AVM has not yet been obliterated must bleed at a higher rate in order to maintain a constant bleeding rate for the entire group. This suggests that, as the AVM's become smaller with radiosurgery and therefore increase in perfusion pressure, they face an increased risk of hemorrhage. This is consistent with the hypothesis generated by our study.

Continuing with this theme, it is true that we did not specify "absolute or relative rates" for patients with previously unruptured AVM's that ruptured and bled several days to weeks after partial embolization. This was purely an observational statement and was not generated by a large study. However, we have become convinced during the treatment of our patients that the more aggressive the embolization the higher the associated risk of hemorrhage. Embolization naturally very nicely converts a larger AVM to a smaller AVM and clearly changes the perfusion pressure proximal to the embolization. The authors go on to argue that "In our recent experience of 185 consecutive "partially" embolized AVM's, nine (4.8%) hemorrhages occurred" and that "This hardly constitutes a 'frequent' occurrence." While nine hemorrhages in 185 patients with partially embolized AVM's do not appear at first glance to be very many, this is in fact erroneous. This impression that a low risk of hemorrhage exists is very misleading because we are missing the denominator: 4.8% of hemorrhages over a 10-year period as opposed to over a 1-week period in the embolized patients is vastly different. A hemorrhage incidence of nearly 5% in partially treated AVM's over a brief postembolization period of only several days is enormous, especially if this frequency persists. Therefore, a 4.8% risk of hemorrhage associated with the partial embolization treatment of an AVM is in fact a very high hemorrhage risk, and we consider this to be partly related to the increased perfusion pressure created by the effects of the embolization.

Finally, the authors offer the explanation that some of these postembolization hemorrhages can be attributed to "inadvertent venous outflow obstruction." We agree with this observation. Obviously, sudden obstruction of venous outflow will increase the perfusion press-
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sure throughout the patent AVM proximal to occlusion to a level approaching systemic arterial pressure. This is a perfect example illustrating the mechanics of our theory.

I would like to gently chide our endovascular colleagues for the lack of long-term outcome studies of patients treated only with partial embolization. Where indeed is the proof of the efficacy of their treatment which we are all aware is not entirely risk-free? My comments are in no way meant to denigrate the important observations presented by the authors, nor do I deny the very valuable contributions of endovascular and radiosurgical treatments in the management of AVM’s, but I believe it behooves all of us to look at the efficacy as well as the risk of each individual treatment modality and determine how each is used to maximize efficacy of treatment and minimize morbidity and mortality for an individual patient. The complexity of AVM’s is such that a great deal of additional study is required to achieve a more complete understanding of the hemodynamics of these fascinating lesions.

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References

Cervical Spondyloptosis

To THE EDITOR: I was intrigued by the report by Drs. Bhojraj and Shahane (Bhojraj SY, Shahane SM: Posttraumatic cervical spondyloptosis at C6-7 with late-onset cord compression: a new clinical entity. Case report. J Neurosurg 77:792-794, November, 1992). It depicts an extraordinarily rare clinical entity very well and points up the fallacy of waiting for a second case before reporting a single instance of what may be a unique observation.

Twenty-one years ago, I treated a 7-year-old boy whose radiological pictures showed “spondyloptosis” at C-7, with C-7 and C-6 lying anterior to T-1 and T-2. Myelography indicated a 50% narrowing of the thecal sac at the kink in the spinal canal, but neurological examination revealed only a mild increase in tone of the lower extremities. The boy complained of pain around his shoulders. Flexion-extension cervical films (gently done), lateral view, showed a fixed deformity. This patient came from an obscure social background, he was a foster child, and there was no known neck trauma; however, he had been abused as an infant.

I performed an anterior excision of C-7. T-1, and T-2, did not use an anterior bone graft, but did follow up with a posterior fusion (wire and bone) of C-6 and T-3. During a 6-year postoperative period, the patient did very well, then he disappeared into some other jurisdiction.

Cervical spondyloptosis in children must be extremely rare and certainly appears intimidating, but it is eminently correctable.

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Response: I wish to thank Dr. Amacher for acknowledging the rarity of this entity. I share his concern about not reporting such rare disorders, in the interest of the subject.

The case he managed almost 21 years ago seems to be very similar to the one we described in presentation and end result; however, the etiology and management protocol were different. With regard to the etiology, it is interesting that in our case we also initially entertained the possibility of child abuse, but this was subsequently ruled out. As mentioned in the article, there was a classic history of birth trauma with associated palsy of the upper limb.

Concerning the management protocol, we believe that cervical spondyloptosis is an extreme form of cervical kyphosis, with loss of anterior structural support, which becomes severely unstable after any anterior decompressive surgery (corpectomies). Any form of pure posterior construct in such situations is unlikely to provide significant and continued stability and, although achieving good initial recovery, may risk the development of a progressive kyphotic deformity and delayed neurological deficits, especially in immature spines. Such cases, we feel, should be reconstructed anteriorly using solid autologous strut bone grafts to ensure a satisfactory long-term result.

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Distal Catheter Lengthening

To THE EDITOR: I am writing to express objection to the paper by Drs. Goldenberg and Pritz (Goldenberg TM, Pritz MB: A simple method for distal catheter lengthening of ventriculoperitoneal shunts. Technical note. J Neurosurg 77:810-811, November, 1992). In describing a method of lengthening the distal catheter of a ventriculoperitoneal shunt, they suggest that a new distal catheter can be passed over a guidewire into the peritoneal cavity and connected to the transected end of the old catheter via a small abdominal or lower thoracic incision. It has been my experience that wherever a connector is inserted into a shunt circuit, scarring occurs. The tubing therefore becomes tethered at that point. The peritoneal catheter is thus tethered both at the proximal end, next to the valve, and at the point of insertion into the peritoneal cavity. As the child grows, this portion of the tubing then tends to come under tension, leading to patient discomfort and the potential for catheter breakage.

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