Stereotactic Radiosurgery for Partially Resected Cerebral Arteriovenous Malformations

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■ OBJECTIVE: **Incomplete microsurgical resection of cerebral arteriovenous malformations (AVM) occurs uncommonly. However, such patients harboring postoperative residual nidi remain exposed to the risk of AVM hemorrhage and are therefore reasonable candidates for further intervention. The goals of this retrospective case-control study are to analyze the radiosurgery outcomes for partially resected AVMs and determine the effect of prior resection on AVM radiosurgery outcomes.**

■ METHODS: **We evaluated a prospective database of AVM patients treated with radiosurgery from 1989–2013. Previously resected AVMs with radiologic follow-up ≥2 years or nidus obliteration were selected for analysis and matched, in a 1:1 fashion and blinded to outcome, to previously unresected AVMs. Statistical analyses were performed to assess relationship between prior resection and AVM radiosurgery outcomes.**

■ RESULTS: **The matching process yielded 88 patients in each of the previously resected and unresected AVM cohorts. In the resected AVM cohort, the actuarial AVM obliteration rates at 3 and 5 years were 47% and 75%, respectively; the rates of radiologic and symptomatic radiation-induced changes (RICs) were 10% and 3%, respectively; and the annual postradiosurgery hemorrhage risk was 1.1%. The lack of prior AVM resection ($P < 0.001$) and superficial AVM location ($P = 0.009$) were independent predictors of radiologic RIC. The actuarial rates of obliteration ($P = 0.849$) and postradiosurgery hemorrhage ($P = 0.548$) were not significantly different between the resected and unresected AVM cohorts.**

■ CONCLUSIONS: **Radiosurgery affords a reasonable risk-to-benefit profile for incompletely resected AVMs. For those with a small-volume residual nidus after resection, radiosurgery should be considered an effective alternative to repeat resection.**

INTRODUCTION

Microsurgical resection is a standard of care for patients with cerebral arteriovenous malformations (AVMs) and offers the greatest likelihood of complete obliteration and immediate freedom from future AVM hemorrhage.[1-5] Resection of superficial AVMs of the cerebrum or cerebellum yields excellent obliteration rates of over 90%.[6] However, postoperative obliteration rates for deep-seated AVMs of the basal ganglia, thalamus, and brainstem are more variable, ranging from 67% to 100%.[7] Incomplete resection of an AVM may occur intentionally, when further resection could convey a substantial neurologic deficit to the patient or, inadvertently, when additional nidus is not seen at the time of resection. In one study of deep AVMs, complete resection was accomplished in only 71% of patients.[8]

Key words
- Gamma Knife
- Intracranial arteriovenous malformations
- Microsurgery
- Radiosurgery
- Stroke
- Vascular malformations

Abbreviations and Acronyms
ARUBA: A Randomized Trial of Unruptured Brain AVMs
AVM: Arteriovenous malformation
CI: Confidence interval
CT: Computed tomography
IRB: Institutional Review Board
MRI: Magnetic resonance imaging
RBAS: Radiosurgery-based AVM score
RIC: Radiation-induced changes
SAIVM: Scottish Audit of Intracranial Vascular Malformations
SD: Standard deviation
SM: Spetzler-Martin
VRAS: Virginia Radiosurgery AVM Scale

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Although incomplete resection is less common, the presence of a residual nidus subjects the patient to a persistent long-term risk of AVM hemorrhage.[9] As such, intervention is typically warranted for incompletely resected AVMs, particularly if the original indication for resection was AVM rupture.

Stereotactic radiosurgery offers a minimally invasive alternative to repeat craniotomy for the management of a postoperative residual nidus.[10-24] However, the effect of prior surgical intervention on an AVM's radiobiology and the response of a partially resected nidus to radiosurgery have not been thoroughly analyzed. Therefore the aims of this retrospective case-control study are to 1) evaluate the outcomes after treatment of partially resected AVMs with radiosurgery, 2) identify the predictors of obliteration and complications after radiosurgery for previously resected AVMs, and 3) determine the effect of prior resection on AVM radiosurgery outcomes.

METHODS

Patient Selection

We retrospectively analyzed a prospective, Institutional Review Board (IRB)-approved database of approximately 1400 AVM patients who were treated with Gamma Knife radiosurgery at the University of Virginia from 1989 to 2013. The inclusion criteria for the case cohort (i.e., resected AVM cohort) were 1) prior AVM surgical resection; 2) sufficient data regarding baseline patient characteristics, AVM features, radiosurgery parameters, and postradiosurgery outcomes; and 3) minimum of 2 years' radiologic follow-up after radiosurgery, except for patients with complete AVM obliteration on angiography or magnetic resonance imaging (MRI), who were included even if the duration of radiologic follow-up was less than 2 years. The exclusion criteria were 1) prior AVM treatment with embolization, 2) prior neurosurgical intervention other than AVM resection, and 3) AVM treatment with volume- or dose-staged radiosurgery. The inclusion and exclusion criteria for the control cohort (i.e., unresected AVM cohort) were the same as those for the case cohort, except only patients with previously unresected AVMs were selected.

Data and Variables

Baseline data extracted from directed chart review included 1) patient characteristics, 2) AVM angioarchitectural features, and 3) radiosurgery parameters. Patient variables were gender, age, and presenting symptoms. AVM angioarchitectural features were prior AVM resection, size (maximum diameter and volume of nidus), prior hemorrhage, location (eloquent vs. noneloquent, superficial vs. deep), venous anatomy (number of draining veins, superficial only vs. deep component), and presence of associated aneurysms. Eloquent locations were sensorimotor, language, and visual cortex, hypothalamus and thalamus, internal capsule, brainstem, cerebellar peduncles, and deep cerebellar nuclei.[5] Deep locations were basal ganglia, thalamus, and brainstem.[25] On the basis of the aforementioned variables, the Spetzler-Martin (SM) grade, modified radiosurgery-based AVM score (RBAS), and Virginia Radiosurgery AVM Scale (VRAS) were determined for each patient.[5,25,26]

Radiosurgical Approach

Our Gamma Knife radiosurgery technique for the treatment of AVMs has been previously described.[27] Before 1991, MRI was not routinely used in addition to cerebral angiography for radiosurgical planning. After 1991, a combination of MRI and angiography were used to improve the spatial accuracy of radiosurgical planning. Before June 1994, dose planning was performed using the Kula software. From July 1994 onwards, dose planning was performed using the Gamma Plan software. The radiosurgery variables were margin dose, maximum dose, isodose line, and number of isocenters.

Radiologic and Clinical Follow-up

Radiologic follow-up after radiosurgery was composed of serial MRIs at 6-month intervals for the first 2 years and then annual MRIs thereafter. Additional neuroimaging, either computed tomography (CT) or MRI, was performed in patients experiencing new or worsening neurologic symptoms. All follow-up imaging was reviewed by a neuroradiologist and neurosurgeon at the University of Virginia, regardless of where it was obtained.

AVM obliteration was defined as a lack of flow voids on MRI or as the absence of abnormal arteriovenous shunting on angiography. Angiography was performed to confirm obliteration diagnosed on MRI or to plan further intervention(s) for a residual AVM nidus. Radiation-induced changes (RIC) were defined as perinidal T2-weighted hyperintensities on follow-up MRI.[28] The time interval between radiosurgery and RIC development and the duration of RIC were noted. Symptomatic RICs were defined as RICs associated with new or worsening neurologic deterioration, and permanent RICs were defined as persistently symptomatic RIC by the most recent clinical follow-up. Latency period hemorrhage was defined as AVM-related hemorrhage after radiosurgery, irrespective of a change in the patient's neurologic status, on CT or MRI. Postradiosurgery cyst formation was defined as the development of a cystic cavity within or adjacent to the brain region occupied by the original nidus on CT or MRI.

Clinical follow-up was composed of clinic and hospital records from the University of Virginia, correspondence with patients' local physicians, and notes from referring institutions. Patients were categorized as neurologically improved, unchanged, or deteriorated by comparing the neurologic condition at the most recent clinical follow-up encounter to the baseline neurologic status at the time of radiosurgery. Patients with seizures at presentation were categorized as follows: 1) seizure remission was defined as the complete resolution of baseline seizures, 2) seizure improvement was defined as seizure remission or reduced seizure frequency, 3) seizure worsening was defined as an increase in the frequency or intensity of baseline seizures, or 4) unchanged seizure status. De novo seizures were defined as the onset of seizures after treatment with radiosurgery in patients without seizures at presentation.

Matching Process and Statistical Analysis

Statistical analyses were performed with the IBM SPSS 20 software program. All statistical tests were 2-sided. Statistical significance was defined as a P value <0.05. Data were presented as frequency for categorical variables and as mean with standard deviation (SD) or median with range for continuous variables. Radiologic and clinical outcomes after radiosurgery were reported as frequencies. Using propensity score matching with an R program, the previously resected AVMs (case cohort) were matched, in a 1:1 fashion