Radiosurgery for Cerebral Arteriovenous Malformations in Elderly Patients: Effect of Advanced Age on Outcomes After Intervention

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■ OBJECTIVE: **Cerebral arteriovenous malformations (AVM) are infrequently diagnosed and treated in elderly patients (age, >60 years). We hypothesize that, in contrast to AVM surgical outcomes, radiosurgery outcomes are not adversely affected by increased age. The goals of this case-control study are to analyze the radiosurgery outcomes for elderly patients with AVMs and determine the effect of elderly age on AVM radiosurgery outcomes.**

■ METHODS: **We evaluated a prospective database of patients with AVMs treated with radiosurgery from 1989 to 2013. Elderly patients with AVM (age, ≥60 years) with radiologic follow-up of ≥2 years or nidus obliteration were selected for analysis, and matched, in a 1:1 fashion and blinded to outcome, to adult nonelderly patients with AVM (age, <60 years). Statistical analyses were performed to determine actuarial obliteration rates and evaluate the relationship between elderly age and AVM radiosurgery outcomes.**

■ RESULTS: **The matching processes yielded 66 patients in each of the elderly and nonelderly AVM cohorts. In the elderly AVM cohort, the actuarial AVM obliteration rates at 3, 5, and 10 years were 37%, 65%, and 77%, respectively; the rates of radiologically evident, symptomatic, and permanent radiation-induced changes were 36%, 11%, and 0%, respectively; the annual hemorrhage risk after radiosurgery was 1.1%, and the AVM-related mortality rate was 1.5%. Elderly age was not significantly associated with AVM obliteration, radiation-induced changes, or hemorrhage after radiosurgery.**

■ CONCLUSIONS: **Advanced age does not appear to confer appreciably worse AVM radiosurgery outcomes, unlike its negative effect on AVM surgical outcomes. Thus, when an AVM warrants treatment, radiosurgery may be the preferred treatment for elderly patients.**

INTRODUCTION

Most cerebral arteriovenous malformations (AVMs) are diagnosed and treated by the third or fourth decades of life (1, 2, 11). Therefore, diagnosis and treatment of an AVM in elderly patients (age, ≥60 years) is relatively uncommon, although increases in life expectancy over time may result in more frequent AVM diagnoses in the elderly population. A recent meta-analysis of risk factors for AVM hemorrhage found increasing age to be an independent predictor of hemorrhage risk (29). Given the poorer neurological reserve in elderly patients compared with their younger counterparts, stroke secondary to AVM rupture may be particularly devastating in this vulnerable patient population (23).

AVM surgical outcomes have been previously shown to be poorer in elderly patients (9, 28, 30). A similar inverse correlation between favorable outcome and age has been described for AVM radiosurgery (40, 52). However, the negative effect of age on post-treatment outcomes in patients with AVM when treated by radiosurgery has not been consistently observed in prior analyses

Key words
- Age groups
- Elderly
- Gamma knife
- Intracranial arteriovenous malformations
- Radiosurgery
- Stroke
- Vascular malformations

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

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Citation: World Neurosurg. (2015).
http://dx.doi.org/10.1016/j.wneu.2015.05.012

*Journal homepage: **www.WORLDNEUROSURGERY.org***

*Available online: **www.sciencedirect.com***

(6, 10, 12-14, 16-18, 20, 25-27, 33, 36, 41, 53). Furthermore, a study evaluating the radiosurgery outcomes in elderly patients with AVM has not been performed. Therefore, we hypothesize that, unlike surgical outcomes, increased patient age does not significantly worsen AVM radiosurgery outcomes. In this retrospective case-control study, our aims are to 1) analyze the outcomes after the treatment of elderly patients with AVM by radiosurgery, 2) define the predictors of obliteration and radiosurgery-induced complications after radiosurgery for AVMs in elderly patients, and 3) determine the effect of elderly age on AVM radiosurgery outcomes.

METHODS

Patient Selection

We retrospectively evaluated a prospective, institutional review board-approved, database of approximately 1400 patients with AVM who were treated with gamma knife radiosurgery at the University of Virginia from 1989 to 2013. The inclusion criteria for the case (elderly) cohort were 1) patient age 60 years or more, 2) sufficient data regarding baseline patient characteristics, AVM features, and outcomes after radiosurgery, and 3) minimum of 2 years of 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 inclusion criteria for the control (nonelderly) cohort were the same as those for the case cohort, except only adult (<60 years) patients with AVM, but at least 18 years of age, were selected. Patients treated with volume- or dose-staged radiosurgery were excluded.

Data and Variables

Baseline data, including 1) patient characteristics, 2) AVM angioarchitectural features, and 3) radiosurgery parameters, were extracted from chart review. Patient variables were gender, age, and presenting symptoms. AVM angioarchitectural features were prior interventions (surgical resection and/or embolization), 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 included sensorimotor, language, and visual cortex, hypothalamus and thalamus, internal capsule, brainstem, cerebellar peduncles, and deep cerebellar nuclei (45). Deep locations included basal ganglia, thalamus, and brainstem (52). Based on these variables, the Spetzler-Martin grade, modified radiosurgery-based AVM score (RBAS), and Virginia radiosurgery AVM scale (VRAS) were determined for each nidus (45, 49, 52).

Our gamma knife radiosurgery technique for AVMs has been previously described (50). Before 1991, radiosurgical planning did not routinely include the use of MRI in addition to angiography. After 1991, both MRI and angiography were used to enhance the spatial accuracy of radiosurgical planning. From 1989 until June 1994, dose planning was performed using the Kula software, and from July 1994 onward, dose planning was performed using the Gamma Plan software. The radiosurgery variables were prescription dose, maximum dose, isodose line, and number of isocenters.

Radiologic and Clinical Follow-up

Radiologic follow-up after radiosurgery was comprised of serial MRIs every 6 months for the first 2 years, and then annual MRIs after 2 years of follow-up. Additional neuroimaging, either computed tomography (CT) or MRI, was performed in patients with neurological decline after treatment. 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, on MRI, by a lack of flow voids or, on angiography, by an absence of anomalous arteriovenous shunting. Angiography was used to confirm obliteration based on MRI or to plan further intervention(s) for a residual nidus. Radiation-induced changes (RIC) were defined on follow-up MRI by perinidal T_2-weighted hyperintensities (54). The time interval between radiosurgery and the emergence of RIC and the duration of RIC were noted. Symptomatic RIC was defined as RIC accompanied by new or worsening neurological status. Permanent RIC was defined as symptomatic RIC without resolution of the associated neurological deterioration by the most recent clinical follow-up. Latency period hemorrhage was defined by follow-up CT or MRI as the occurrence of AVM-related hemorrhage after radiosurgery, with or without a change in the patient's neurological status. Cyst formation after radiosurgery was defined by CT or MRI as the development of a cystic cavity within or adjacent to the region occupied by the original nidus.

Clinical follow-up was comprised of a combination of clinic and hospital records from the University of Virginia, correspondence with patients' local physicians, and notes from other referring institutions. After comparing a patient's neurological condition at the most recent clinical follow-up encounter to the baseline neurological status at the time of radiosurgery, patients were classified as neurologically improved, unchanged, or deteriorated. In the patients who died, the patient age at death, time interval between radiosurgery and death, and cause of death were noted. Patients with seizures at presentation were classified as follows, after comparing the seizure status at the most recent clinical follow-up to the baseline seizure status: 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. Patients without seizures at presentation were classified as having de novo seizures if they developed new seizures after radiosurgery.

Matching Process and Statistical Analysis

Statistical analyses were performed with the IBM SPSS 20 software (SPSS, Armonk, New York) program. All statistical tests were 2-sided. Statistical significance was defined as a P value less than 0.05. Data were presented as frequency for categorical variables and as mean with standard deviation (SD) and median with range for continuous variables. Radiologic and clinical outcomes after radiosurgery were reported as frequencies. Using propensity score matching, the elderly patients with AVMs (case cohort) were matched, in a 1:1 fashion and blinded to outcome, to nonelderly patients with AVMs (control cohort) based on prior surgical resection, prior embolization, prior AVM hemorrhage, nidus volume, eloquent AVM location, number of draining veins, presence