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Clinical Study

Hypofractionated stereotactic radiosurgery for treatment of cerebral arteriovenous malformations: outcome analysis with use of the modified arteriovenous malformation scoring system

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ABSTRACT

Radiosurgery has long been an accepted modality for definitive treatment of cerebral arteriovenous malformations (AVM). Efforts to improve the therapeutic ratio for this indication include use of staged volume procedures and hypofractionation. This study reviews our experience with a cohort of patients treated with hypofractionated radiosurgery. Over a 3 year period, 38 patients harboring 39 cerebral AVM were treated with hypofractionated stereotactic radiotherapy. Seventeen of these patients presented due to hemorrhage, four were asymptomatic unruptured lesions and the remainder were symptomatic unruptured lesions. The median AVM volume was 11.43 cc and median modified Radiosurgery-Based Arteriovenous Malformation Score (mRBAS) was 2.02. The median follow-up was 7.32 years. Four patients harboring four AVM were lost to follow-up before a result could be ascertained leaving 35 AVM for analysis. Excellent outcomes (AVM obliteration without new deficits) occurred in 17 of 34 (50%) patients and in 18 of 35 (51%) AVM treated. AVM obliteration was seen in 26 of 35 (74%) lesions treated. Two patients died during the follow-up period (6%). A poor result (major deficit without obliteration) was seen in one patient. Of 19 patients harboring AVM with mRBAS >2.0, an excellent outcome was achieved in eight (42%). Hypofractionation for cerebral AVM can result in satisfactory obliteration rates, but with risk of significant complications commensurate with mRBAS. Further study of this technique will be needed to ascertain the degree of incremental improvement, if any, over other radiosurgery treatment methods.

1. Introduction

Intracranial arteriovenous malformations (AVM) are complicated congenital vascular lesions that can remain asymptomatic throughout a patient's life, or present with significant symptoms such as intracranial hemorrhage, seizure, or headache. While recent studies have advocated for conservative management for incidentally noted unruptured AVM [1,36], the preferred management for AVM not meeting these circumstances remains unclear. Treatment options include microsurgical resection, embolization, single fraction stereotactic radiosurgery, hypofractionated stereotactic radiosurgery, or a combination of these treatment modalities.

Single fraction stereotactic radiosurgery and hypofractionated stereotactic radiosurgery have both been explored as non-invasive treatment options for AVM. Single fraction treatments have successfully been utilized for smaller lesions [33,59], but this technique is felt to be less than ideal for larger lesions [18,29,58,57]. Larger AVM have proven less amenable to single fraction treatments, resulting in lower obliteration rates and increased morbidity [8]. These results have prompted further exploration into alternative radiosurgery approaches including staged volume radiosurgery [46,4,10,15,18,27] and hypofractionated stereotactic radiosurgery [3,6,8,28,30,50,51,55,58] with or without prior embolization.

Conventional fractionated techniques have been used in the past for large cerebral AVM, although reports of their use have been sporadic [25,44,49]. More recently, hypofractionated treatments have been described using both gantry-based isocentric linear accelerator (LINAC) and non-isocentric LINAC devices.

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The optimal number of fractions and dose per fraction has not been established. Various groups have looked at using two to seven fractions of 5 to 7 Gy per fraction for total doses of 12 to 42 Gy [3,6,8,29,30,50,55,51], with improved obliteration rates observed with larger dose per fraction. We report the long term results of our institutional experience treating patients with AVM using hypofractionated stereotactic radiotherapy. Results were then compared to historical series using the modified Radiosurgery-Based Arteriovenous Malformation Score (mRBAS) [39].

2. Materials and methods

2.1. Patient selection

Patients were referred to the Regional Center for Radiosurgery Services at Kaiser Los Angeles Medical Center, USA. Patients were counseled regarding treatment options including surgical resection, embolization, radiosurgery and multimodality therapy by a team comprised of neurological surgeons, interventional radiologists, and radiation oncologists.

2.2. Treatment technique

All patients were treated using a LINAC (Novalis, Brainlab, Helmstetten Germany) using mini-multileaf collimation at 6 MeV energy with a single isocenter technique. A repositionable mask fixation technique was used as previously described [2,53]. Lesions were contoured on basis of high resolution MRI. BrainScan version 5 software (BrainLab AG, Helmstetten, Germany) was used for dose planning.

The median dose/fractionation regimen was 35 Gy in five consecutive daily 7 Gy fractions prescribed to a median prescription isodose line of 80%. This fractionation schedule is equivalent to a biological effective dose of 116.67 Gy and an equivalent 2 Gray dose (EQD2) of 70 Gy, assuming an alpha/beta of 3.0 [24,43]. This is equivalent to 17.3 Gy in a single fraction at an alpha/beta ratio of 3. A median of 100% of the contoured volume of the lesions was covered by the prescription isodose line.

2.3. Clinical follow-up and data analysis

Following treatment, patients were followed with serial MRI, typically at 6 month intervals followed by cerebral angiography for final assessment of response. The modified Rankin Scale was used to assess pre and post-treatment functional status.

Data was collected and analyzed retrospectively. Patients lost to follow-up were excluded from analysis to allow comparison with prior published reports utilizing RBAS [39,40,52]. To assess correlation between the 2002 version of the RBAS and the 2008 version of the RBAS, scores for all patients were calculated using both techniques. The scores were highly correlated with a Pearson R = 0.998. As there was no significant difference between the methods, it was elected to use the 2008 mRBAS as the basis for all calculations.

Univariate analysis employed Fisher's exact, Spearman rank order, Wilcoxon Matched Pairs and Mann–Whitney U tests where appropriate.

This work was approved by the Southern California Permanente Medical Group Institutional Review Board.

3. Results

3.1. Demographic characteristics

From April 2004 through June 2007, 38 patients harboring 39 AVM were treated using hypofractionated stereotactic radiotherapy. For the single male patient with two AVM, the mRBAS scores for each AVM were 1.34 and 1.37. Four patients harboring four AVM were lost to follow-up within 3 years following the treatment, leaving 35 AVM in 34 patients available for review. Of the patients lost to follow-up, two had lesions with mRBAS <2, and two had mRBAS >2. Demographic characteristics of patients completing follow-up are presented in Table 1.

3.2. Patient characteristics in relation to mRBAS

Univariate analysis was undertaken to assess the relation between mRBAS scores and pre-treatment demographic characteristics not utilized in calculation of the mRBAS. No significant correlation was seen for sex, side of lesion, prior hemorrhage or Spetzler–Martin score. A correlation was noted between mRBAS and pre-treatment embolization, with embolization being utilized more in patients with higher mRBAS. Results are presented in Table 2.

3.3. Median follow-up

Following treatment, patients were followed with MRI, typically at 6 month intervals. Follow-up angiography was obtained if MRI was suggestive of AVM obliteration. The median follow-up for patients at time of data collection was 8 years (range: 0.9–10.36 years).

3.4. AVM response

Of 39 lesions treated, 23 demonstrated complete obliteration by angiography at the end of the data collection period. Six lesions were shown to not be obliterated. Radiographic imaging from an illustrative patient is presented in Figure 1.

Outcomes binned to mRBAS are presented in Table 3. The overall obliteration rate in this series was 74% with 51% achieving excellent results. For AVM with mRBAS>2, overall obliteration rate was 72% with excellent results in 44%. There appeared to be no significant difference in excellent outcomes or overall obliteration rates with differing sizes in this series.

Pre-treatment embolization did not appear to correlate with the likelihood of obtaining an excellent clinical result, nor did it correlate with likelihood of obliteration in this series (Table 4).

Univariate analysis was performed to assess mRBAS against outcome parameters. These are presented in Table 5. In this series,

Table 1
Demographic characteristics of AVM patients treated with hypofractionated stereotactic radiosurgery with completed follow-up

Patients	34
AVM	35
Male	22
Female	13
Age	43.8 (14.5–61.5 years)
Side of AVM	16 left, 19 right
Primary presenting symptom	
Intracranial hemorrhage	17
Seizures	5
Headache	5
Focal motor deficit	1
Visual deficits	1
Sycope	2
Vertigo	1
Incidental asymptomatic	4
AVM volume	11.43 (1.3–108.6 cc)
AVM mRBAS	2.01 (0.66–11.95)
AVM prior embolization	8, 23%
Total margin dose in 5 fractions	35 (28–35 Gy)
Pre-treatment modified Rankin Scale score	1 (0–4)

Data are presented as number or median (range) or number, %.
AVM = arteriovenous malformation, mRBAS = modified Radiosurgery-Based Arteriovenous Malformation Score.