ORIGINAL RESEARCH

Evaluation of the radiosurgical treatment of cerebral arteriovenous malformations: a retrospective single-center analysis of three decades

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ABSTRACT

Background Gamma Knife radiosurgery (GKRS) in the treatment of arteriovenous malformations (AVMs) is still controversially discussed.

Objective To present long-term follow-up data on patients after Gamma Knife radiosurgery for cerebral AVMs.

Methods Overall, 516 patients received radiosurgery for cerebral AVMs between 1992 and 2018 at our department, of whom 265 received radiosurgery alone and 207 were treated with a combined endovascular-radiosurgical approach. Moreover, 45 patients were treated with a volume-staged approach. Two eras were analyzed, the pre-modern era between 1992 and 2002 and the modern era thereafter.

Results In GKRS-only treated patients, median time to nidus occlusion was 3.8 years. Spetzler–Ponce (SP) class was a significant predictor for time to obliteration in the whole sample. Median time to obliteration for the combined treatment group was 6.5 years. Patients in the pre-modern era had a significantly higher obliteration rate than those treated in the modern era. Overall, the calculated yearly hemorrhage risk in the observation period after first GKRS was 1.3%. Permanent post-radiosurgical complications occurred in 4.9% of cases but did not differ between the treatment groups or treatment eras. The obliteration rate was significantly lower and the hemorrhage rate was higher in volume-staged treated patients than in conventionally treated patients.

Conclusion GKRS is an effective treatment option for SP class A and B cerebral AVMs. After combined endovascular-radiosurgical treatment, the outcome of selected SP class C AVMs aligns with that of SP class B lesions. Both the combined therapy and radiosurgery alone constitute sound methods for treatment of cerebral AVMs.

INTRODUCTION

Although radiosurgery is widely accepted in the management of cerebral arteriovenous malformations (AVMs), its relevance in the treatment of larger or ruptured AVMs is still controversial.[1–3] Besides the employment of conservative management, which is recommended by some authors,[1–3] a combined treatment approach where endovascular embolization is followed by radiosurgery or volume-staged radiosurgery is discussed in large high grade AVMs. The combined endovascular-radiosurgical approach has been described as safe and effective in several studies.[4 5] In contrast, other studies reported lower obliteration rates owing to recanalization or obscuring of the Gamma Knife radiosurgery (GKRS) target by the embolic agent.[6 7] The efficacy and safety of the volume-staged approach is the subject of current research.[2 8–10] Besides evaluating the different treatment options, clinicians treating cerebral AVMs have been challenged since the ARUBA study by Mohr *et al* was published.[11] Although there were many limitations to the ARUBA study which have been repeatedly criticized by experts, the discourse on treating unruptured AVMs has become more divisive. Thus, continuous evaluation of treatment success has become vital.[11 12] To evaluate the treatment success of radiosurgery in a large AVM sample and contribute to the scientific debate, we conducted this long-term follow-up evaluation.

METHODS

Patient sample and data evaluation

The study was approved by our institutional review board. Since analysis of data was done retrospectively, patient consent was not obtained. Overall, 516 patients with AVMs were treated with GKRS between 1992 and 2018 in our department. To reduce selection bias, we included every patient in our sample who underwent at least one GKRS for a cerebral AVM in our department. Data were obtained by analysis of patient records, multimodal imaging at diagnosis, radiosurgical treatment plans, and follow-up imaging and evaluated retrospectively. Cases were rated according to clinical and radiological assessment scores (table 1).[13–16] We divided our study sample into two eras, pre-modern and modern, as others have done previously.[17 18]

Table 1 provides an overview of the patient and AVM characteristics and highlights statistically significant differences among the treatment groups. Overall, 516 patients received radiosurgery for cerebral AVMs in our department, of whom 265 received radiosurgery alone and 207 were treated with a combined endovascular-radiosurgical approach. Forty-four patients received other

Table 1 Patient and arteriovenous malformation (AVM) characteristics (n=472)

	GKRS/Endo (n=207)	GKRS (n=265)	Group differences P value
Gender			
Female	100 (48%)	124 (47%)	
Male	107 (52%)	141 (53%)	0.743
Age (years)			
Median (range)	34 (6–75)	40 (7–80)	0.001
KPS at diagnosis (%)			
Median (range)	80 (20–100)	90 (30–100)	0.001
Hemorrhage before first intervention			
Yes	93 (45%)	81 (31%)	
No	114 (55%)	184 (69%)	0.001
Venous drainage			
Deep	145 (70%)	165 (62%)	
Superficial	62 (30%)	100 (38%)	0.077
Eloquence			
Eloquent	125 (60%)	144 (54%)	
Not eloquent	82 (40%)	121 (46%)	0.188
AVM volume at diagnosis (cm^3)			
Median (range)	5.3 (0.1–66.0)	2.3 (0.1–42.0)	0.001
RBAS			
Median (range)	1.3 (0.2–5.3)	1.3 (0.2–4.2)	0.130
VRAS			
Median (range)	2 (0–4)	2 (0–4)	0.001
Spetzler–Ponce			
A	64 (31%)	130 (49%)	0.001
B	83 (40%)	109 (41%)	
C	60 (29%)	26 (10%)	
Multiple GKRS			
Yes	78 (38%)	68 (26%)	0.005
No	129 (62%)	197 (74%)	

GKRS, Gamma Knife radiosurgery; GKRS/Endo, combined endovascular and radiosurgical treatment; KPS, Karnofsky Performance Status Scale; RBAS, radiosurgery based AVM score; VRAS, Virginia Radiosurgery AVM Scale.

multimodal treatment combinations including microsurgery before GKRS and were excluded from our analysis. In general, patients in the combined treatment group were younger, were more often diagnosed with hemorrhages prior to first intervention, had a higher Spetzler–Ponce (SP) score and thus presented in a clinically worse condition. For two patients, Karnofsky Performance Status at diagnosis could not be retrospectively evaluated due to missing information from hospitals abroad.

Radiosurgical technique

Patients were treated with a Leksell Gamma Knife (Model B until 2011/Perfexion from 2012 onwards; Elekta AB, Stockholm, Sweden). KULA (Elekta AB) was used as the planning software between 1992 and August 1997 and GammaPlan (Elekta AB) was used from August 1997 onwards. For treatment planning, three imaging modalities were performed under stereotactic conditions including MRI with high-resolution T2-weighted scans and time-of-flight MR angiography, contrast-enhanced CT angiography (CTA) together with bone window and biplane rotational angiography. MRI was performed on either a 1.5T or 3T scanner, according to patients' compatibility. The target comprised the AVM nidus on MRI, CTA, and angiography-registered imaging without additional margins. In the case of volume-staged treatment, the treatment plan was separated into volumetric stages to minimize dose overlap between stages.

Follow-up and outcome evaluation

Clinical and radiological outcome was evaluated. A death register comparison showed that 36 of 472 patients (8%) died from other causes at the time of evaluation. Seven patients (7/472) died as a result of their AVM, resulting in a mortality rate of 1.5% in the whole series. After 2002, the mortality rate dropped to 0.7%. The median follow-up time after first intervention was 5.5 (0.6–32.0) years. Thirty percent of patients presented with a follow-up time >10 years. The total observation period was 2673.7 years. After GKRS, patients were followed with MRI every year until obliteration and at 3–5-year intervals after obliteration. Obliteration on MRI was defined as an absence of flow voids on T1- and T2-weighted images.[18 19] Obliteration was confirmed by biplane catheter angiography or MRI results depending on the patients' wishes. If a residual nidus was still diagnosed on MRI 2 years after GKRS, angiography was planned under stereotactic conditions and another GKRS was performed.[18 19]

Statistical analysis

Statistical calculations included the Mann–Whitney U test and the χ^2 test. The effect of every variable on the outcome and occlusion rates was first analyzed with univariable regression analysis. Variables having a significant impact were then tested with multivariable regression models. Median time to obliteration and hemorrhage rate were measured with Kaplan–Meier estimators and life tables. Using Breslow testing, patients were divided into groups according to different characteristics and compared. A p value <0.05 was considered statistically significant. IBM SPSS Statistics for Windows Version 25.0 (IBM, Armonk, New York, USA) was used. Patients lost to follow-up were included in the study but excluded from the outcome analysis.

RESULTS

Differences between treatment groups and treatment era

Differences among the treatment groups and treatment eras are shown in table 1 and table 2. Significantly more patients (108/190, 56%) underwent combined endovascular-radiosurgical treatment in the pre-modern era than in the modern treatment era (99/282, 35%; p=0.001). Moreover, in the radiosurgery only group, a significant increase existed in SP class A patients treated in the modern treatment era than in those treated in the pre-modern era (p=0.042). In the combined group, the median number of embolizations before GKRS was 2 (1–12). No significant difference existed in the number of embolizations before GKRS between the pre-modern and modern era in our sample. N-butylcyanoacrylate was the predominant embolic agent in both treatment eras and remains the preferred one in our department.

Table 2 shows the historic difference in Gamma Knife parameters of the first Gamma Knife treatment between the pre-modern era (1992–2002) and the modern Gamma Knife era (2003–2018). Statistically significant differences among the two groups are highlighted. In two patients data about the first Gamma Knife parameters were missing due to treatment

Table 2 Overview of Gamma Knife radiosurgery (GKRS) parameters for first GKRS of the pre-modern and modern Gamma Knife era (n=472)

	Pre-modern era (1992–2002) (n=190)	Modern era (2003–2018) (n=282)	Group differences P value
Treatment volume, cm^3 Median (range)	3.6 (0.1–21.0)	2.5 (0.1–16.6)	**0.006**
Isodose line, % Median (range)	50 (34–85)	50 (40–65)	0.369
Prescription dose, Gy Median (range)	18 (8–30)	19 (11–22)	**0.001**
Central dose, Gy Median (range)	36 (16–50)	38 (23–48)	**0.001**

Significant differences are shown in bold type.

in another Gamma Knife centre. In those cases radiosurgical parameters of the first treatment at our center were included. It should be noted that the prescription dose with 30 Gy in the radiosurgery only group is one extreme value.

Post-interventional hemorrhage and complications

In the combined treatment group, 12 of 207 patients (6%) had a hemorrhage after their first partial embolization—that is, before their first radiosurgical treatment. The rate of hemorrhage after embolization did not differ significantly between patients with a hemorrhage and those without a hemorrhage before the first intervention. However, patients with peri-embolization hemorrhage underwent significantly more embolization procedures than those without hemorrhage (p=0.028). Overall, 9% of our patients (35/388) had a hemorrhage after their first radiosurgical treatment. For 12 of those cases, a scheduled appointment for further treatment was not kept by the patient. Nineteen patients received endovascular treatment and eight underwent microsurgery owing to hemorrhage after their first radiosurgical treatment. There was no difference in the hemorrhage rate between the GKRS only and combined treatment groups.

The calculated yearly hemorrhage risk in the observation period after first GKRS was 1.3%. Several risk factors for hemorrhage could be identified (table 3). Kaplan–Meier analysis estimated time to hemorrhage after first GKRS did not differ significantly between SP classes (figure 1A). After GKRS, the total rate of persisting radiation-associated complications for both treatment groups was 4.9% (19/388 patients) and included the occurrence of radiologically diagnosed edema or late onset cyst formation with or without new neurological symptoms. The rate of radiation-associated complications did not differ between the different treatment groups or treatment eras. The occurrence of neoplasia was observed in the course of the lifetime of five patients. Due to the contralateral location of their occurrence, four of these tumors were not regarded as radiation induced.[20] In one patient an oligodendroglioma (WHO II) developed adjacent to the radiation site. Fulfilling Cahan's criteria, this neoplasm was classified as radiation induced.[20]

Table 3 shows risk factors for hemorrhage after stereotactic radiosurgery identified by univariable regression analysis and the χ^2 or Mann–Whitney U tests as appropriate. High SP class and Spetzler–Martin grade, high AVM diameter, low marginal dose of first GKRS, high radiosurgery-based AVM score (RBAS) and Virginia Radiosurgery AVM Scale (VRAS), multiple GKRS treatments, long time between first and last GKRS and pre-modern era were identified as significant risk factors in the first level of our analysis. Multivariable regression was calculated only for variables that were significant predictors in univariable regression analysis. After multivariable regression analysis, only time between first and last GKRS remained as a significant predictor for hemorrhage.

Table 3 Assessment of risk factors for post-radiosurgical hemorrhage (n=388)

	χ^2 or Mann–Whitney U test	Univariable regression P value	Multivariable regression P value
Spetzler–Ponce class	0.019	0.015	0.562
Spetzler–Martin grade	0.011	0.008	0.605
AVM diameter	0.003	0.001	0.234
RBAS	0.014	0.002	0.147
VRAS	0.004	0.003	0.455
Multiple GKRS Yes/no	0.033	0.033	0.068
Time between first and last GKRS	0.021	0.001	0.001
Treatment era	0.025	0.025	0.145
Marginal dose (grouped <20 Gy, 20Gy, >20 Gy)	0.027	0.029	0.354
Number of feeders	0.202	0.053	
Age	0.757	0.895	
Gender	0.240	0.241	
Venous drainage	0.291	0.292	
Initial KPS		0.416	
Hemorrhage before treatment	0.786	0.786	
Cerebral circulation	0.512	0.166	

GKRS, Gamma Knife radiosurgery; KPS, Karnofsky Performance Status; RBAS, radiosurgery-based AVM score; VRAS, Virginia Radiosurgery AVM Scale.

Multiple GKRS treatments and truly volume-staged cases

A third of our patients (146/472, 31%) received multiple GKRS treatments. Of these cases, one was due to multilocular AVMs and 100/472 (21%) because of incomplete occlusion. The majority received two radiosurgical treatments (74/100, 74%). In rare cases, a maximum of four radiosurgical treatments were applied. In the combined treatment group, significantly more patients received multiple GKRS treatments. Overall, the median time between the first and second GKRS was 2.4 (0.1–22.6) years. This time range includes patients who for many years did not adhere to their follow-up schedule and were diagnosed with a residual or only partially treated AVM many years after first GKRS. Only 45 of 146 patients with multiple GKRS qualified as truly volume-staged treatments (supplementary table S1). Among volume-staged cases alone, the median time between the treatments was 2.1 (0.9–10.3) years. The median treatment volume of this subgroup was three times that of conventionally treated patients. Eleven volume-staged patients (24%) had hemorrhage after radiosurgery. Three (7%) of 45 volume-staged patients died as a result of AVM hemorrhage and 5 (11%) had persisting radiosurgery-associated complications. The median time to obliteration was 11.2 years (95% CI 7.7 to 14.6). Obliteration rates after 3, 5, and 10 years were 20%, 29%, and 49%, respectively.

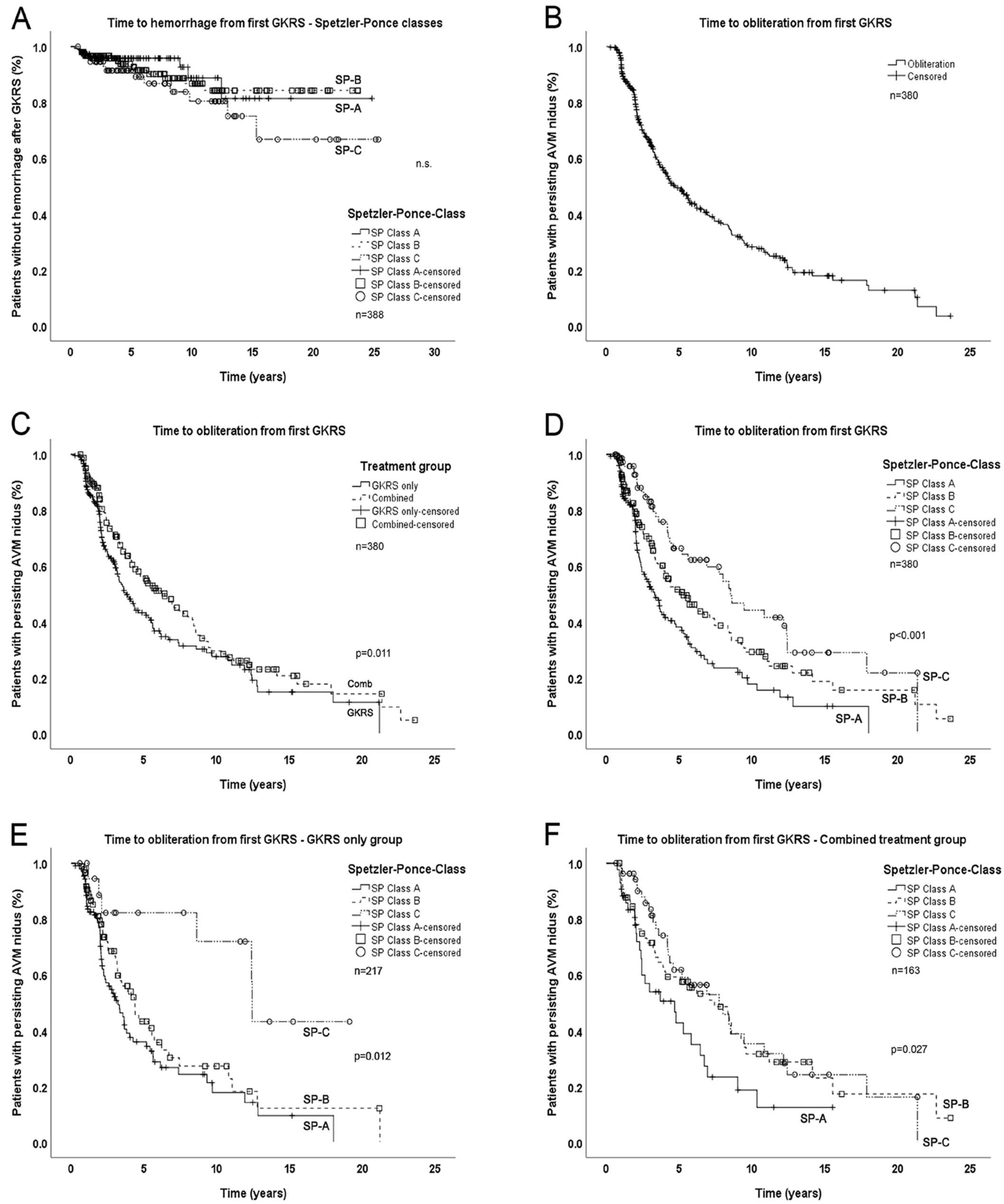

Figure 1 (A) Time to hemorrhage after first Gamma Knife radiosurgery (GKRS) treatment for Spetzler–Ponce (SP) classes A, B, and C (n=388). No significant difference was found. For SP class C patients, a tendency towards a shorter time to hemorrhage was found in a subanalysis; however, this trend was only of borderline significance in patients in the combined treatment group only (p=0.079; data not shown). (B) Time to obliteration from first GKRS for all 380 patients for whom radiological follow-up was available. Both treatment groups are included. The obliteration rates were 44%, 56%, and 74% after 3, 5, and 10 years, respectively. (C) Time to obliteration from first GKRS for the two treatment groups separately. In GKRS only treated patients (n=217), the median time to nidus occlusion was 3.8 years (95% CI 3.0 to 5.6) and the obliteration rates after 3, 5, and 10 years were 51%, 63%, and 74%, respectively. In contrast, the median time to obliteration for the combined treatment group was 6.5 years (95% CI 4.8 to 8.1 years) with obliteration rates of 36%, 49%, and 73% after 3, 5, and 10 years, respectively. (D) Time to obliteration from first GKRS for each SP class, showing a significantly shorter time to obliteration in SP class A lesions (p=0.001, n=380). For SP classes A, B, and C, the median times to occlusion from first GKRS treatment were 3.3 years (95% CI 2.5 to 4.1), 5.3 years (95% CI 3.7 to 6.9), and 8.5 years (95% CI 6.7 to 10.4), respectively. Among SP class A patients the obliteration rates after 3, 5, and 10 years were 57%, 69%, and 84%, respectively; in SP class B patients the rates were 42%, 54%, and 72%, respectively; and in SP class C patients the obliteration rates were 24%, 38%, and 58%, respectively. (E) Time to obliteration from first GKRS in patients treated by radiosurgery only. SP class C arteriovenous malformations (AVMs) showed a significantly longer time to obliteration (p=0.012, n=217) and lower obliteration rates. The median times to obliteration for SP classes A, B, and C were 3.3, 4.4, and 12.4 years with obliteration rates of 80%, 72%, and 28%, respectively, 10 years after first GKRS. (F) Time to obliteration from first GKRS in patients in the combined treatment group only. SP class A AVMs showed a significantly shorter time to obliteration (p=0.027, n=163) and higher obliteration rates. Of note, after combined treatment with embolization followed by radiosurgery, the outcome of selected initial SP class C AVMs aligned with that of SP class B lesions. The median times to obliteration for SP classes A, B, and C were 4.7, 7.4, and 7.7 years with obliteration rates of 88%, 67%, and 68%, respectively, 10 years after first GKRS.

Overall obliteration and outcome-influencing risk factors

The actuarial median time to obliteration from the first GKRS treatment was 4.7 years (95% CI 3.8 to 5.6) (figure 1B). No significant difference existed in the median time to obliteration between the two treatment eras. However, a subanalysis of the two treatment groups revealed significant differences (figure 1C). For the whole study sample, the SP class was a significant predictor for the median time to obliteration as well as obliteration rates (figure 1D). However, the predictive value of the initial SP classification was dependent on the treatment group (figure 1E and F). After combined treatment with embolization followed by radiosurgery, the outcome of selected initial SP class C AVMs aligned with that of SP class B lesions in our series (figure 1F).

Next, we performed regression analyses to further identify predictive factors for AVM obliteration. In the radiosurgery only group, univariable regression analysis (n=217) showed that a low SP class score (p=0.011), small AVM diameter (p=0.002), and pre-modern era treatment (p=0.005) were positive predictive factors for obliteration. Among the combined treatment groups (n=163), neither of these variables significantly affected obliteration. Among 380 patients, in the multivariable regression analysis, AVM diameter (p=0.010) and pre-modern era treatment (p=0.005) were significant positive predictors for obliteration.

DISCUSSION

Limitations

We have reported on long-term follow-up data of a large series of AVM patients. The vast majority of patients in our study were treated in the pre-ARUBA era. Limitations of our study include its retrospective nature and its center and treatment bias. Because of our hospital's treatment policy in the pre-ARUBA era, we could not provide data on the natural history of cerebral AVMs.

Differences between treatment groups and treatment era and the evolution of radiosurgical AVM treatment

Patients who underwent combined treatment were generally younger, more often diagnosed with hemorrhages before the first intervention, and more often associated with higher SP scores. Our observed higher rate of previous hemorrhage among our combined treatment cohort compared with the GKRS only cohort is not generally observed in other samples.[6 21] Moreover, patients in our combined sample underwent a rather high number of embolizations before GKRS.[5 7 22] This may be explained by the fact that our hospital functions as a tertiary referral center, accepting patients pretreated at other centers as well. However, in the course of a changing treatment algorithm, the ratio of radiosurgically-only treated patients increased during the observation period. In addition, the overall radiosurgical treatment plan underwent a significant change. In our pre-modern era, the range of the prescription dose was much higher with doses up to 30 Gy, reflecting the early approach to the novel technique at that time. Later on, in the modern era, a treatment algorithm was already established, resulting in a smaller range of the prescription dose. Consequently, in our cohort the modern era is characterized by smaller single treatment volumes but higher median prescription doses. Similar developments but a considerable increase in isocenters in the modern era have been described and are in line with our findings.[17 18]

Low post-radiosurgical hemorrhage and complication rates in a pre-ARUBA sample add to the relativization of ARUBA

Radiosurgery-associated complications, including edema, cyst, and radiation reaction, have significantly decreased over time.[18 23 24] Permanent post-radiosurgical complication rates range between 2.5% and 6% in the literature and are thus similar to our reported complication rate of 4.9%. However, since the ARUBA study by Mohr *et al* was published in 2014, clinicians treating cerebral AVMs have been challenged.[11]

As has been criticized before, the rate of hemorrhages and post-interventional complications in the interventional arm of ARUBA was clearly higher than that reported in the literature.[25] The hemorrhage rates of the interventional and conservative cohorts in this randomized multicenter trial were 24.5% and 5.6%, respectively.

In contrast, we found an overall hemorrhage rate after first GKRS of 9% of all patients, corresponding well with previously published series.[17 18 23 24 26] Although the overall hemorrhage rate among the non-interventional ARUBA cohort was lower than that of our post-interventional rate, our follow-up was significantly longer. Consequently, the yearly hemorrhage rate of 1.3% in our observation period after first GKRS is in line with the recent literature and is significantly lower than that in the non-interventional arm of the ARUBA study (2.2%).[17 18 23 24 26] Of note, according to a meta-analysis of 3923 patients, untreated AVMs have an overall yearly hemorrhage rate of 3.0%.[27]

Moreover, AVM baseline characteristics were obviously more favorable in the ARUBA study sample, including more than two-thirds of patients with SP class A lesions, compared with 40% in our cohort. The yearly hemorrhage risk after GKRS among SP class A patients in our study was 1.1%. Furthermore, the number of patients in the ARUBA study treated by radiosurgery (n=31) or by a combination of embolization and radiosurgery (n=15) was comparatively small. Predictors for post-radiosurgical hemorrhage, such as large AVM diameter and volume, high SP class, RBAS or VRAS, which were identified in our analysis, have also been reported previously.[18 23 24]

However, our significantly higher rate of post-radiosurgical hemorrhage in the pre-modern era differs from other results.[17 18] The higher hemorrhage rate among patients treated in the pre-modern era in our study may be due to significantly higher SP classes among the pre-modern treatment group. Our finding that patients requiring multiple GKRS are at a higher risk of hemorrhage may be explained by a longer time of vulnerability in those patients.

At the European Consensus Conference on Unruptured Brain AVMs Treatment in 2017, it was concluded that the ARUBA results could not be applied equally for all unruptured AVMs and for all treatment modalities. Furthermore, to balance the risk of hemorrhage against that of treatment, there are sufficient indications to treat unruptured AVMs of Spetzler–Martin grade 1 and 2.[12] Our findings further support the role of radiosurgery in AVM treatment and relativize the ARUBA results.

Truly volume-staged cases

Forty-five patients were treated by a volume-staged strategy mainly due to an exceedingly large AVM volume. However, in some cases, despite a moderate volume, the localization was decisive for choosing the volume-staged approach to minimize the risk of Radiation-induced changes (RIC) in our sample. Consequently, in our volume-staged cohort, patients had a significantly higher SP class and significantly higher RBAS and VRAS scores than the remaining sample. The rate of patients undergoing embolization before radiosurgery in our sample is higher than that in other volume-staged cohorts.[9 10 28] The median time interval between the first and second stage was 25 (10–123) months, which is considerably longer than the median time interval reported in recent studies but represents the cautious approach of our center.[8–10 28]

Our post-radiosurgical hemorrhage rate of 24% confirmed the findings of previous volume-staged studies ranging from 14% to 28%.[8] This rate is considerably higher than that of our remaining sample and appears to confirm the dependence of post-GKRS hemorrhage risk on AVM size, as described earlier. This rate includes several patients who did not have their second planned treatment for many years. Previous studies analyzing the outcome of volume-staged treated patients reported obliteration rates between 33% and 86%.[8 29] An obliteration rate of 49% at 10 years from first GKRS in our volume-staged cohort confirms the relative efficacy of this technique in treating more complex AVMs.[9 10 28] Because of the still high post-radiosurgical hemorrhage risk in volume-staged patients, a general recommendation for treatment cannot be made. In our opinion, the management of high-grade AVM patients can only be decided on an individual basis in a multidisciplinary setting.

Obliteration after radiosurgery

In larger studies, the obliteration rates 10 years after first radiosurgery ranged from 65% to 78% and corresponded with our findings of 74% among the whole sample. This rate includes patients of all SP classes, as well as volume-staged treated patients. The 10-year obliteration rate for SP class A patients alone was 84%. It is a well-known fact that a large AVM diameter as well as scores including diameter or volume are negative predictors for obliteration.[17 18 24 26] This correlation has also been observed in our sample.

However, in our combined treatment group, after embolization followed by radiosurgery, the median time to obliteration and obliteration rates of initial SP class C lesions aligned with that of class B lesions. These findings clearly demonstrate the positive downsizing effect of pre-GKRS embolization in selected large high-class AVMs.[30] In the literature, the use of pre-(radio) surgical embolization is still controversial due to the concern that embolization may add risk.[31] In recent years, the advent of new embolic agents has slightly changed the endovascular AVM management. Several groups reported good outcomes with targeted pre-radiosurgical Onyx embolization.[31 32] However, in our department, N-butylcyanoacrylate was the predominant embolic agent in both treatment eras since both senior cerebrovascular neurosurgeons (GB, AG) had been accustomed to its use in AVM embolization, as others have also described.[31 32]

Although there was no difference in the actuarial median time to obliteration between the two treatment eras, significantly more patients reached obliteration in the pre-modern era. Previously published studies also describe higher obliteration rates among patients treated in the earlier era. The authors believed that their contemporary dose plans may be too conformal due to the goal of minimizing radiation-induced changes although they found no significant difference between the two eras.[17 18]

In our study, patients treated in the modern era had smaller single treatment volumes but higher prescription doses. Consequently, according to our study, the lower obliteration rate in the modern era can neither be explained by differences in AVM baseline characteristics nor in prescription dose. Moreover, embolization before radiosurgery has been claimed to reduce obliteration rates.[6 7] However, the rate of prior embolizations was higher in our pre-modern cohort than in our modern cohort. In line with other authors, we suggest that obliteration rates in contemporary cohorts are lower than previous cohorts for the following two reasons. First, the follow-up time of more recent cases is usually shorter than that of historic cases, confounding the outcome analysis. There was no difference in the obliteration rates between the two eras when the cohorts were limited to a minimum follow-up of 3 years. Second, the indications for radiosurgery have broadened during the last decades owing to a considerable gain of experience in AVM radiosurgery. Hence, more complex AVMs requiring multiple GKRS are often treated in modern cohorts.[17 18]

CONCLUSION

GKRS is an effective treatment option in the management of SP class A and B cerebral AVMs. Our findings suggest that, after combined treatment with radiosurgery and prior embolization, the outcome of the selected SP class C AVMs aligns with that of SP class B lesions. Volume-staged radiosurgery for large AVMs is relatively effective, but the risk of hemorrhage after GKRS in this subgroup is high. Thus, the management of high grade AVM patients can only be decided on an individual basis in a multidisciplinary setting after accounting for patients' wishes and circumstances.

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