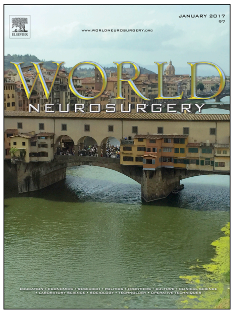
Journal Pre-proof



Does endovascular treatment with curative intention have benefits for treating High-grade AVM versus radiosurgery? Efficacy, safety, and cost-effectiveness analysis

Rebeca Pérez-Alfayate, MD, PhD, Giovanni Grasso, MD, PhD, Cristina Fernández Pérez, MD, PhD, Javier Arias-Díaz, MD, PhD, Kita Sallabanda-Díaz, MD, PhD

PII: S1878-8750(21)00246-1

DOI: https://doi.org/10.1016/j.wneu.2021.02.053

Reference: WNEU 16832

To appear in: *World Neurosurgery*

Received Date: 11 November 2020

Revised Date: 11 February 2021

Accepted Date: 12 February 2021

CRediT author statement

Pérez-Alfayate, R, conceived of the presented idea, designed the study, performed the measurements, collected the analyzed data, and wrote the manuscript. Grasso, G contributed to the writing and editing of the manuscript, Fernández-Pérez, C, processed the data and performed the statistical analysis. Grasso G, Arias-Diaz, J and Sallabanda-Diaz, K, supervised the study. All authors discussed the results and commented on the manuscript.

Does endovascular treatment with curative intention have benefits for treating High-grade AVM versus radiosurgery? Efficacy, safety, and cost-effectiveness analysis

Rebeca Pérez-Alfayate, MD, PhD[1], Giovanni Grasso, MD, PhD[2], Cristina Fernández Pérez, MD, PhD[3], Javier Arias-Díaz, MD, PhD[4], Kita Sallabanda-Díaz, MD, PhD[1].

[1]*Neurosurgery Department. Neuroscience Institute. Hospital Clínico San Carlos, Madrid, Spain.*

[2] *Department of Biomedicine, Neuroscience and Advanced Diagnostics (BiND). University of Palermo, Palermo, Italy.*

[3]*Methodology and Clinical Epidemiology Unit, Preventive Medicine Department. Hospital Clínico San Carlos. Madrid, Spain.*

[4]*Department of Surgery. Medical School. Complutense University, Madrid, Spain.*

Running Title: SRS vs embolization for High Grade AVM

Corresponding Author: Rebeca Pérez-Alfayate, MD. PhD

Department of Neurological Surgery Hospital Clínico San Carlos.

Calle del Profesor Martín Lagos S/N 28040. Madrid, Spain.

Email: rebecap.alfayate@gmail.com/rebper01@ucm.es

Phone number: +34610422197

Does endovascular treatment with curative intention have benefits for treating High-grade AVM versus radiosurgery? Efficacy, safety, and cost-effectiveness analysis

ABSTRACT

BACKGROUND:

The treatment of high-grade arteriovenous malformations (AVMs) remains challenging. Microsurgery provides a rapid and complete occlusion compared to other options, but is associated with undesirable morbidity and mortality.

The aim of this study was to compare the occlusion rates, incidence of unfavorable outcomes, and cost-effectiveness of embolization and stereotactic radiosurgery (SRS) as a curative treatment for high-grade AVMs.

METHODS

A retrospective series of 57 consecutive patients with high-grade AVM treated with embolization or SRS, with the aim of achieving complete occlusion, was analyzed. Demographic, clinical, and angio-architectonic variables were collected. Both treatments were compared for the occlusion rate and procedure-related complications. In addition, a cost-effectiveness analysis was performed.

RESULTS

Thirty (52.6%) patients were men and 27 (47.4%) were women (mean age 39 years). AVMs were unruptured in 43 (75.4%) patients, and ruptured in 14 (24.6%) patients. The presence of deep venous drainage, nidus volume, perforated arterial supply, and eloquent localization were more frequent in the SRS group. Complications such as hemorrhage or worsening of previous seizures were more frequent in the embolization group. No significant differences were observed in the occlusion rates or in the time necessary to achieve occlusion between the groups. The incremental cost-effectiveness ratio for endovascular treatment vs. SRS was $ 53.279.

CONCLUSION

Both techniques achieved similar occlusion rates, but SRS carried a lower risk of complications. Staged embolization may be associated with a greater risk of hemorrhage, while SRS was demonstrated to have a better cost-effectiveness ratio. These results support SRS as a better treatment option for high-grade AVMs.

Key Words: Arteriovenous malformation, Embolization, Endovascular, Radiosurgery, Spetzler-Martin Scale, Stereotactic

Highlights

-Radiosurgery seems to be safer than endovascular embolization when used as a curative treatment for high-grade AVMs.

- In high-grade AVMs, a higher number of staged embolization procedures is associated with an increased risk of bleeding.

- Radiosurgery is more cost-effective than endovascular embolization.

INTRODUCTION

Arteriovenous malformations (AVMs) have an incidence of 1.1/100.000 person-years[1] and are the second major cause of hemorrhagic stroke in young patients. [2,3] An estimate indicated that the annual risk of hemorrhage from unruptured AVMs is 2.4%.[4] In individuals with high-grade AVMs, the annual risk is 1.17 %. [5]

The Spetzler-Martin Scale (SM)[6] has been used to classify AVMs according to their associated surgical risk, thus identifying a possible management by separating patients into two distinct groups: low-grade and high-grade AVMs. Usually, the term low-grade refers to grades I and II, and high grade refers to grades IV and V. However, grade III did not fit into these two groups. Lawton et al.[7] subdivided grade III into four groups: S1V1E1 (grade III-), S2V1E0 (grade III), S2V0E1 (grade III+), and S3V0E0 (grade III*). S1V1E1 (S: size, V: venous drainage, E: eloquent area) seems to have a low surgical risk, similar to grades I and II. Therefore, from a practical perspective, AVMs could be classified into 2 categories, leaving S1V1E1 within the low-grade group, and including the other grade III lesions in the high-grade group.

Currently, there are four treatment options for AVM: microsurgery, embolization, stereotactic radiosurgery (SRS), and conservative management. Regarding low-grade lesions, there has been some consensus on the therapeutic method to be used[8].

Conversely, there has been a great deal of controversy regarding high-grade AVM management[9]. In particular, debate exists whether one of more treatments can worsen the natural history of high-grade AVMs since the partial treatment of these lesions could increase the incidence of hemorrhage up to 10.4%[10].

Microsurgery is a challenging option in high-grade AVMs. In these cases, considering the high morbidity and mortality[11], surgery should be reserved for patients with previous hemorrhage, with existing significant permanent deficits, progressive neurological deficits related to vascular steal, or an associated arterial or intranidal aneurysm[10]. SRS is an effective management strategy for selected AVMs[12]. The main drawback of this technique is its latency time, or delayed treatment effect, which exposes the patient to a higher risk of bleeding during this period.[13,14] Another important limitation is the risk of radiation-related injury, but advancements in SRS techniques such as hypofractionated stereotactic radiotherapy (HST) or stage volume SRS (SVR) have been proven to minimize this hazard.[15]

Embolization is a common adjuvant to surgery or SRS, providing good results[16]. However, in recent years, due to the significant developments in embolization materials and approaches, endovascular procedures have become more effective with the potential for application with a curative intent[17,18]. However, embolization can be followed by a substantial rate of complications, and its safety and efficacy are supported by an unsatisfactory retrospective series.[19]

Currently, treatment of high-grade AVMs is usually performed using a combination of these treatment options. Several studies have compared the results of a single technique with the natural history of AVMs or microsurgery, concluding that partial treatment of AVMs offered no protection from hemorrhage and is indeed associated with an elevated incidence of hemorrhage.[10] However, multiple angio-architectonic, clinical, and hemodynamic parameters should be taken into account since they could predict AVM rupture risk or treatment outcome after each management modality. [4,20–25]

Multidisciplinary and case-to-case consensus decision of an experienced team is the normal practice to manage AVMs[26,27], especially for high-grade AVMs. Most of these cases are treated multimodally, but some cases are treated using a single technique, as mentioned earlier, due to the technical advances in the different treatment modalities.[15-17] To the best of our knowledge, SRS and embolization used separately for curative treatment of high-grade AVMs have not yet been compared. Therefore, we sought to compare the efficacy, safety, and cost-effectiveness of these treatments when applied with a curative intention on high-grade AVMs.

METHODS

All procedures performed in this study were in accordance with the ethical standards of the Institutional Review Board (IRB) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study protocol was approved by the institutional review board (17/026-E_Tesis). Informed consent was waived due to the retrospective nature of the study.

Patient population

A retrospective series of 144 consecutive patients with high-grade AVMs treated between 2000 and 2015 were analyzed. High-grade AVMs were defined as those that matched SM grades IV and V and SM grade III fitting the Lawton´s high microsurgical risk criteria.[7] Patients with high-grade AVM treated with embolization or SRS as single curative modality treatment, with a minimum follow-up of 4 years were included. This latency period was considered sufficient to achieve an effect following SRS. [28,29] Patients who had not been assessed at least with an annual imaging test, such as a conventional arteriography, and MRI 4 years after starting the treatment were also excluded. Similarly, patients who underwent microsurgery as the main approach for the management of AVM were excluded from the study. However, patients who underwent surgical procedures to manage hemorrhage-related complications, such as ventriculostomy or intracranial hematoma evacuation, and patients who had a flow-related aneurysm embolization before radiosurgery were included.

Treatment

Patients in the endovascular group were treated with staged embolization using onyx as an embolic agent. Patients in the SRS group were treated with a single dose (mean dose 16 Gy, range: 15–16.5 Gy) or HST techniques (5 × 6 Gy, 7 x 3 Gy, and 2 x 10). For single-dose treatment, the LINAC Precise system (Elekta, Estocolmo) was used with the Philips SRS 200 mechanical system (Shelton/CT, EE). The electron beam energy was *6 MeV*.

Outcomes

Patient outcomes were assessed by analyzing the main clinical and angio-architectonic variables previously suggested as risk factors for complications, hemorrhage, or poor outcomes[4,6,11,20–25,30]. Results and treatment characteristics were assessed using data obtained from the medical records, pre-treatment arteriography, and 4-year follow-up conventional arteriography and MRI. The main variables were occlusion rate, defined as the complete occlusion of the AVM observed in a conventional angiogram at the 4-year follow-up, complication rate, and clinical status. The latter was evaluated using the modified Rankin scale (mRS). The mRS was dichotomized into good outcome (mRS=0-2) or bad outcome (mRS=3-6).

Statistical Analysis

For the statistical analyses, the quantitative variables were summarized as mean and standard deviation. The qualitative variables were presented with their frequency distribution. A normality test was performed to determine whether to apply parametric or non-parametric tests of the quantitative variables to the hypothesis comparison. The Shapiro-Wilk test was used in most of the hypothesis test groups, since N < 50. For the parametric tests, Student's t-test and analysis of variance were used to compare the means between two groups or 3-or-more categories, respectively. In the non-parametric tests, the Mann–Whitney test was used when the categorical variable was distributed in two groups and the Kruskal–Wallis test was used when there were three or more categories.

In many of the studies on the independence of variables, the chi-square test was not valid because the frequencies at the cross-table boxes were < 5. Accordingly, Fisher's exact test was applied. Logistic regression tests were used to identify the risk predictors of hemorrhage and unfavorable outcomes. In addition, receiver operating characteristics (ROC) curves were obtained. A cost-effectiveness analysis was performed considering effectiveness as the complete occlusion rate. Cost values were obtained from the Cost and Management Control Service. Overall treatment costs included the costs of the planning imaging tests, inpatient hospital stay, treatment procedure, and outpatient follow-up.

In the endovascular group, the costs included each embolization session. Since the treatment was planned as a staged procedure, the final cost was obtained by multiplying the mean cost by the number of procedures performed. For the SRS group, the costs were obtained from the mean cost of the hypofractionated procedures. Costs from the endovascular and SRS groups also included the treatment time, annual imaging tests, and outpatient follow-up. Furthermore, for cases that required embolization of a flow-related aneurysm, the final cost was calculated by adding up each cost.

Statistical analyses were performed using IBM SPSS statistics version 23 (IBM Corp; USA). Differences with a probability higher than 95% ($p<0.05$) were considered significant.

RESULTS

After applying the inclusion and exclusion criteria, the final sample size was 57 patients. Thirty (52.6%) were men and 27 (47.4%) were women, with a mean age of 39 years (range, 4–89 years). Forty-three (75.4%) AVMs were unruptured, while 14 (24.6%) presented with rupture. Among the bleeding cases, 7 (14%) presented with intraventricular hemorrhage. Seven AVMs (12.2%) were discovered incidentally. The main presenting features were seizure (49.1%), headache (24.6%), and blood steal phenomenon (12.3%), often combined in the same patient at admission. The mean AVM diameter was 4.99 cm (range, 3.4–8 cm). In 80.7% of the cases, the AVM affected an eloquent area, and in 60% it was associated with deep venous drainage. Subject characteristics, clinical features, and AVM angio-architectonic variables are summarized in Table 1.

Embolization was performed in 26 (45.6%) patients, while 31 (54.4%) patients underwent SRS. The AVM locations for the two groups are shown in Table 2.

Most of the patients in the SRS group were treated with HSR, but 4 underwent single-dose treatment. The average of isocenters used was 2 (range, 1–3), and a total dose of

18.3 (± 3.08) Gy was applied. The embolization group was treated with an average of 3.91 procedures (± 4.01).

Overall, both groups were comparable in age, sex, and most of the clinical and angio-architectonic variables. However, some statistically significant differences were observed. In particular, seizures at diagnosis (p=0.05), eloquent location (p=0.009), perforated arterial supply (p=0.004), and deep venous drainage (p=0.038) were more frequently found in the SRS group than in the embolization group (Table 3).

Among the patients, 31 (54.4%) presented with complications related to treatment (Table 4); hemorrhage in 14 cases (24.5%), worsening or new onset of seizures in 6 cases (10.5%), and ischemic events in 5 cases (8.8%) were observed. Cyst or radio-necrosis, edema, and recanalization of the AVMs occurred in 3.5% of cases each. In the SRS group, one patient presented with a radiation-induced cyst and another with radionecrosis. Symptomatic edema was observed in one SRS-treated case and in one case immediately after endovascular embolization. AVM recanalization occurred in 2 cases after complete endovascular embolization, and was seen at the 2-year follow-up. AVMs in the embolization group presented with a statistically significant number of complications (p=0.05) (Table 4). In particular, we found a higher incidence of hemorrhage and seizure related to treatment (p=0.007 and p=0.019, respectively), and a higher need for salvage surgery for complications (p=0.05) (Table 4). The higher risk of hemorrhage in the embolization group was related to both AVM nidus diameter and the number of drainage veins (p = 0.039 and p = 0.042, respectively), while the number of feeders was the variable associated with bleeding in the SRS group (p = 0.002).

Overall, complete AVM occlusion was achieved in 38 cases (66.7%). No statistically significant differences were observed in the occlusion rate between the groups (p=0.184). In addition, mRS at the 4-year follow-up was not significantly different between the groups (p=1.00). The time required to achieve AVM occlusion was higher in the SRS group than in the embolization group (mean 934.43 days vs. 458.08), although this difference did not reach statistical significance (p=0.326). These findings are summarized in Table 5.

A binary logistic regression model was adjusted to evaluate factors that could be associated with the occurrence of hemorrhage. The variables included were those showing statistically significant differences between both treatment groups, and at the same time, associated with the risk of hemorrhage. Accordingly, seizures at presentation, type of treatment, presence of vascular eloquence, nidus volume, eloquent location, presence of perforated arterial supply, and deep venous drainage were considered. We found that embolization treatment (odds ratio [OR] 0.142, 95% confidence interval [CI]: 0.021-0.983; p=0.037) and presence of vascular eloquence (OR 5.44, 95% CI: 1.03-28.66; p=0.046) were variables independently associated with the occurrence of hemorrhage. Data plotted on the ROC curve showed an acceptable discrimination (area under the curve =0.775, p=0.002, 95% CI: 0.828-0.919). Figure 1 depicts these findings.

A binary logistic regression analysis showed that eloquent location and vascular eloquence were independent variables for a poor prognosis (OR not determined, CI 95% 0.000; p=0.002; OR 0.084, CI 95%: 0.010-0.737, p=0.005, respectively). Superficial venous drainage was identified as an independent protective factor (OR: 0.061, 95% CI: 0.006-0.653, p=0.006). However, the ROC curve did not show good discrimination (area under the curve =0.474, p=0.769).

In the cost-effectiveness analysis, effectiveness was defined as the complete occlusion rate. A summary of the results is shown in Figure 2. The incremental cost-effectiveness ratio (ICER) was 53.279, suggesting that complete occlusion with embolization of AVM would increase the cost by approximately 53.279 USD compared with SRS.

DISCUSSION

AVMs represent relatively rare cerebral lesions that may be associated with significant neurological morbidity and mortality. Their management may require a multidisciplinary approach, including surgery, endovascular embolization, and SRS. From their natural history, we know that the annual risk of hemorrhage is between 2% and 4%, with a variability of 1%–33%, when considering the location and anatomical features[31,32]. During the first year after hemorrhage, the risk of re-bleeding varies from 6% – 16%. [33] In light of these observations, the decision to treat a ruptured brain AVM is less controversial than the decision to treat an unruptured AVM[34,35]. In recent years, AVMs have been treated nonsurgically by embolization and SRS with growing results. When possible, surgical resection is often preferred because it can provide removal of the lesion and eliminate the risk of future bleeding. However, surgical resection of AVMs presents perioperative morbidity and mortality, the incidence of which increase with the number of SM grades[36,37]. In this scenario, a small AVM, deeply located and/or in eloquent locations, can be safely treated by SRS. Targeted endovascular embolization can be a solution for an AVM that has bled, because it may decrease the risk of subsequent hemorrhage and reduce radioresistant spots during the latency period following SRS or allow a subsequent complete microsurgical excision[10].

To date, there is no consensus regarding the management of high-grade AVMs[10,38,39,40] Several studies suggest that the relative risk of hemorrhage in high-grade AVMs compared to that in low-or intermediate-grade AVMs remains controversial [5,10,39].

Curative treatment of high-grade AVMs is rarely a realistic goal[41]. Ideally, the definitive treatment would be a complete eradication of the vascular malformation; however, the risks of operative morbidity and mortality are known to range between 17% and 38.4%[6,7,10, 42,43]. To compound the situation, the results of the ARUBA trial (a randomized trial of unruptured brain AVMs) have suggested that medical management is superior to interventional therapy for unruptured AVMs[3]. Although the conclusion of this trial has become almost controversial[44], we have to deal with this evidence, which has had a concrete effect on physicians' decision-making regarding the treatment of unruptured AVMs. Accordingly, the dilemma for treating high-grade AVM still exists, and data pertaining to the outcomes of conservative management versus intervention for these vascular lesions are both limited and conflicting. The TOBAS trial aims to compare the conservative versus interventional treatment for unruptured AVMs in terms of stroke and death from any cause at 10 years[45].

In this retrospective study, we evaluated the results of a series of high-grade AVMs treated by SRS or embolization, each used with a curative intention, and compared the efficacy, safety, and cost-effectiveness of both treatments. Overall, we found that perforated arterial supply, deep venous drainage, and eloquent locations, were more frequent in the SRS group, thus increasing the complexity of AVMs in this group compared with those in the embolization group. Although these findings could lead to a worse outcome in the SRS group, embolized patients presented with a higher incidence of hemorrhage and seizure related to treatment, and a higher need for salvage surgery for complications than the patients treated with SRS.

Based on established evidence that the time for AVM closure following SRS varies between 21 and 48 months[28], our cases were monitored for at least 4 years. Of note, Kano et al.[29] described an obliteration rate of 61% at 5 years, increasing to 70% at 10 years. However, extending the observation time if the AVM is still open, may expose SRS-treated AVM to a worse course compared to its natural history[10].

In our series, the most frequent clinical presentation was seizures, although some authors have observed that the most common clinical presentation was hemorrhage[4, 30,46]. However, this discrepancy is due to the fact that most of the reported series investigated low-grade AVMs in which the most frequent diagnosis was bleeding [47,48], while high-grade AVMs tend to clinically manifest as seizures.[49]

Complications rate and bad outcomes

Some scales have been described to predict the risks of complications or bad outcomes of curative treatment with embolization of AVMs, such as the Buffalo, Puerto Rico, and AVM embocure scores [22–24]. In our series, the average number of feeders was 3.32 (±1.9). This value corresponds to a medium risk based on the Puerto Rico and Buffalo scores, and a low risk based on the AVM embocure score. The mean diameter of the feeders was 1.79 (±0.52), corresponding to a low-risk Buffalo score. However, the percentage of complications was 65.4% in the embolization group. The mean number of procedures performed to achieve complete obliteration was 3.91(SD=4.011). Starke et al.[50] observed that staged embolization using more than one procedure is an independent risk factor for complications. Hartmann et al.[51] observed that severe complications occurred when the number of procedures was ≥ 3.4. The number of procedures performed in our series was higher than recommended; thus, the higher rate of complications observed in our experience can be related to the number of occlusion attempts. Accordingly, it should be taken into account that hemorrhage is a well-known and predictable complication of multiple embolization procedures when trying to achieve a complete high-grade AVM occlusion by embolization.

Most of the AVMs in the SRS group were treated with HSR with different planning schemes, considering that the effect of such a treatment is dose-dependent[52]. The clinical target volume was completely covered in 54.8% of cases. In cases where full coverage was not possible, when planning the target volume, we attempted to cover the feeder region of the nidus. Considering that SRS has a concentric proliferative effect on the vessels[53], we hypothesized that by targeting the AVM feeders, the flux inside the vascular lesion would stop. A single dose technique was performed in 4 out of 31 patients, obtaining complete AVM obliteration in one case.

Deep venous drainage has been described as a risk factor for poor outcomes or hemorrhage[32]. Frequently, deep ventricular, paraventricular, and brainstem locations have been associated with exclusive deep venous drains and deep localization, described as a risk factor for hemorrhage[54]. In our series, these associations were not found. However, we observed that the superficial venous system can be a protective factor for hemorrhage, although investigation of this aspect has been scarcely reported in the literature.

Nevertheless, in the present series, we found that the complication rate of SRS or embolization of high-grade AVMs as a single treatment with curative intent, was higher than the results published for microsurgery series[6,11]. Han et al.[10] recommended complete occlusion of the high-grade AVMs using a combination of treatments in cases with previous severe hemorrhage. In the present series of 144 treated high-grade AVMs, only 57 patients were selected for the analysis of the safety and occlusion rate of SRS or embolization as a single treatment. Considering these results, the best management is conservative management, and combined treatment only for some selected cases.

Occlusion Rate

In our series, the overall occlusion rate was 66.7 %. In particular, the occlusion rate was 77% in the embolization group, and 58.1% in the SRS group. However, these differences were not statistically significant. The occlusion rate achieved in our series was higher than that reported in the literature, although the overall clinical complication rate was also greater[19] (Table 3). The opposite findings were observed in the SRS group, where a lower obliteration rate and a substantially lower complication rate were observed.

Our findings, however, are in line with those previously published. In particular, for giant AVM, Chung et al. reported an obliteration rate of 22.8% and 47.5% for dose-staged and volume-staged groups, respectively, with clinical improvement in the symptoms [55]. In addition, Xiao et al. obtained a significant volume reduction in giant AVMs without increasing the risk of hemorrhage[56].

In our study, the average time to achieve AVM occlusion was longer in the SRS group than in the embolization group, although no statistically significant differences were found between both groups. Conceptually, when considering low-grade AVMs, embolization seems to be an immediately effective treatment, similar to microsurgery. However, this is not the case with high-grade AVMs, since embolization used in a staged fashion requires a long period until the treatment is completed. During the time elapsed, high-grade AVMs might be exposed to a high risk of bleeding, similar to that observed for SRS[10].

Cost-effectiveness analysis

Compared to embolization, SRS resulted in a lower economic burden for the treatment of high-grade AVMs. According to our review of the literature, no studies have compared the cost-effectiveness of SRS and embolization. In our analysis, only costs related to non-complicated procedures were included. In the embolization group, the complication rate was 65.4%, and 45% in the SRS group. Therefore, if the additional costs for treating complications had been included (i.e., costs for increased hospital stay, imaging testing, and other procedures), the ICER would have increased substantially. Likewise, the costs derived from salvage surgery, which was more common in the embolization group, were not included. If they had been considered, they would also have raised the ICER.

When comparing our results with those reported in surgical series[6,11,57], neither SRS nor embolization seems to have additional benefit. Conservative treatment or multidisciplinary management should be chosen for selected patients. Nevertheless, SRS seems to be safer than embolization as a single treatment and achieves a similar occlusion rate. Larger prospective studies should be conducted to confirm these findings.

Limitations

The main limitation of this study is its retrospective nature, which could include selection bias. Prospective trials, as the TOBAS study, will provide more consistent information[58]. However, the characteristics of the AVMs for both groups were comparable when considering the analyzed variables. Another limitation is the sample size. However, the incidence of AVMs is estimated to be 1.1/100,000 person-years[1], and much lower than that of high-grade AVM. For instance, in the ARUBA study[3], 62 out of 226 AVMs were SM grade III, 23 were grade IV, and none were grade V. Taken collectively, our 57 high-grade AVMs represent a series-of-note where, for the first time, patients treated with embolization or SRS as an unique intervention with curative intent were analyzed. Finally, the number of ruptured AVMs was lower than that of bleeding lesions. However, the small number of ruptured AVMs (14 cases out of 57) does not add significant bias to the statistical evaluation. In contrast, analysis of unruptured AVMs may provide further insight into these vascular lesions that are more likely to lead to a poor outcome if left untreated[10].

CONCLUSIONS

SRS and embolization of high-grade AVMs as a single treatment with the aim of complete occlusion showed a high incidence of complication, although SRS carries a lower risk of complications, and staged embolization may be associated with a greater risk of hemorrhage. However, both techniques can provide similar occlusion rates, with SRS offering better cost-effectiveness. We believe that our results can provide data for further robust systematic reviews and meta-analyses useful in tailoring more reliable evidence-based treatment algorithms.

DISCLOSURES

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

SOURCES OF FUNDING

No funding was received for this research.

ACKNOWLEDGMENTS

No other persons, besides authors, have made substantial contributions to this manuscript.

Pérez-Alfayate, R, conceived of the presented idea, designed the study, performed the measurements, collected the analyzed data, and wrote the manuscript. Grasso, G contributed to the writing and editing of the manuscript, Fernández-Pérez, C, processed the data and performed the statistical analysis. Grasso G, Arias-Diaz, J and Sallabanda-Diaz, K, supervised the study. All authors discussed the results and commented on the manuscript.

REFERENCES

1. Brown RD, Wiebers DO, Torner JC, O'Fallon WM. Incidence and prevalence of intracranial vascular malformations in Olmsted County, Minnesota, 1965 to 1992. *Neurology*. 1996;46(4):949-952. doi:10.1212/WNL.46.4.949
2. AlKhalili K, Chalouhi N, Tjoumakaris S, Rosenwasser R, Jabbour P. Staged-volume radiosurgery for large arteriovenous malformations: a review. *Neurosurg Focus*. 2014;37(3):E20. doi:10.3171/2014.6.FOCUS14217
3. Mohr JP, Parides MK, Stapf C, et al. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): A multicentre, non-blinded, randomised trial. *Lancet*. 2014;383(9917):614-621. doi:10.1016/S0140-6736(13)62302-8
4. Hernesniemi JA, Dashti R, Juvela S, Vaart K, Niemela M, Laakso A. Natural history of brain arteriovenous malformations: a long-term follow-up study of risk of hemorrhage in 238 patients. *Neurosurgery*. 2008;63(5):823-831.

doi:10.1227/01.NEU.0000330401.82582.5E [doi]

5. Laakso A, Dashti R, Juvela S, Isarakul P, Niemelä M, Hernesniemi J. Risk of hemorrhage in patients with untreated spetzler-martin grade IV and V arteriovenous malformations: A long-term follow-up study in 63 patients. *Neurosurgery*. 2011;68(2):372-377. doi:10.1227/NEU.0b013e3181ffe931
6. ROBERT FS. A proposed grading system for arteriovenous malformations. *JNeurosurg*. 1986;65(4):6483.
7. Lawton MT, Project UBAMS. Spetzler-Martin Grade III arteriovenous malformations: surgical results and a modification of the grading scale. *Neurosurgery*. 2003;52(4):740-749.
8. Potts MB, Lau D, Abla AA, et al. Current surgical results with low-grade brain arteriovenous malformations. *J Neurosurg*. 2015;122(4):912-920. doi:10.3171/2014.12.JNS14938
9. Cockroft KM, Jayaraman M V, Amin-Hanjani S, Derdeyn CP, McDougall CG, Wilson JA. A perfect storm: how a randomized trial of unruptured brain arteriovenous malformations' (ARUBA's) trial design challenges notions of external validity. *Stroke*. 2012;43(7):1979-1981. doi:10.1161/STROKEAHA.112.652032
10. Han PP, Ponce FA, Spetzler RF. Intention-to-treat analysis of Spetzler—Martin Grades IV and V arteriovenous malformations: natural history and treatment paradigm. *J Neurosurg*. 2003;98(1):3-7. doi:10.3171/jns.2003.98.1.0003
11. Lawton MT, Kim H, McCulloch CE, Mikhak B, Young WL. A supplementary grading scale for selecting patients with brain arteriovenous malformations for surgery. *Neurosurgery*. 2010;66(4):702-713; discussion 713. doi:10.1227/01.NEU.0000367555.16733.E1

12. Pollock BE, Flickinger JC, Lunsford LD, Maitz A, Kondziolka D. Factors Associated with Successful Arteriovenous Malformation Radiosurgery. *Neurosurgery*. 1998;42(6):1239-1244. doi:10.1097/00006123-199806000-00020

13. van Beijnum J, van der Worp HB, Buis DR, et al. Treatment of Brain Arteriovenous Malformations. *JAMA*. 2011;306(18):2011. doi:10.1001/jama.2011.1632

14. Kano H, Kondziolka D, Flickinger JC, et al. Aneurysms increase the risk of rebleeding after stereotactic radiosurgery for hemorrhagic arteriovenous malformations. *Stroke*. 2012;43(10):2586-2591. doi:10.1161/STROKEAHA.112.664045

15. Pollock BE, Kline RW, Stafford SL, Foote RL, Schomberg PJ. The rationale and technique of staged-volume arteriovenous malformation radiosurgery. *Int J Radiat Oncol*. 2000;48(3):817-824. doi:10.1016/S0360-3016(00)00696-9

16. Chen C-J, Ding D, Lee C-C, et al. Embolization of Brain Arteriovenous Malformations With Versus Without Onyx Before Stereotactic Radiosurgery. *Neurosurgery*. August 2020. doi:10.1093/neuros/nyaa370

17. Iosif C, Mendes G, Saleme S, et al. Endovascular transvenous cure for ruptured brain arteriovenous malformations in complex cases with high Spetzler-Martin grades. *J Neurosurg*. 2015;122(5):1229-1238. doi:10.3171/2014.9.JNS141714.Disclosure

18. Zaki Ghali MG, Kan P, Britz GW. Curative Embolization of Arteriovenous Malformations. *World Neurosurg*. 2019;129:467-486. doi:10.1016/J.WNEU.2019.01.166

19. Wu EM, El Ahmadieh TY, McDougall CM, et al. Embolization of brain arteriovenous malformations with intent to cure: a systematic review. *J*

Neurosurg. 2019:1-12. doi:10.3171/2018.10.JNS181791

20. Wegner RE, Oysul K, Pollock BE, et al. A modified radiosurgery-based arteriovenous malformation grading scale and its correlation with outcomes. *Int J Radiat Oncol Biol Phys*. 2011;79(4):1147-1150.

21. Huang Z, Peng K, Chen C, Zeng F, Wang J, Chen F. A Reanalysis of Predictors for the Risk of Hemorrhage in Brain Arteriovenous Malformation. *J Stroke Cerebrovasc Dis*. 2018;27(8):2082-2087. doi:10.1016/j.jstrokecerebrovasdis.2018.03.003

22. Dumont TM, Kan P, Snyder K V, Hopkins LN, Siddiqui AH, Levy EI. A proposed grading system for endovascular treatment of cerebral arteriovenous malformations: Buffalo score. *Surg Neurol Int*. 2015;6:3-7806.148847. eCollection 2015. doi:10.4103/2152-7806.148847 [doi]

23. Feliciano CE, de León-Berra R, Hernández-Gaitán MS, Rodríguez-Mercado R. A proposal for a new arteriovenous malformation grading scale for neuroendovascular procedures and literature review. *P R Health Sci J*. 2010;29(2):117-120. http://www.ncbi.nlm.nih.gov/pubmed/20496526. Accessed March 31, 2019.

24. Lopes DK, Moftakhar R, Straus D, Munich SA, Chaus F, Kaszuba MC. Arteriovenous malformation embocure score: AVMES. *J Neurointerv Surg*. 2016;8(7):685-691. doi:10.1136/neurintsurg-2015-011779 [doi]

25. Neidert MC, Lawton MT, Mader M, et al. The AVICH score: a novel grading system to predict clinical outcome in arteriovenous malformation–related intracerebral hemorrhage. *World Neurosurg*. 2016;92:292-297.

26. Davies JM, Yanamadala V, Lawton MT. Comparative effectiveness of treatments for cerebral arteriovenous malformations: trends in nationwide outcomes from

2000 to 2009. *Neurosurg Focus*. 2012;33(1):E11. doi:10.3171/2012.5.FOCUS12107

27. Cenzato M, Boccardi E, Beghi E, et al. European consensus conference on unruptured brain AVMs treatment (Supported by EANS, ESMINT, EGKS, and SINCH). *Acta Neurochir (Wien)*. 2017;159(6):1059-1064. doi:10.1007/s00701-017-3154-8
28. Awad AJ, Walcott BP, Stapleton CJ, Ding D, Lee C-C, Loeffler JS. Repeat radiosurgery for cerebral arteriovenous malformations. *J Clin Neurosci*. 2015;22(6):945-950. doi:10.1016/j.jocn.2015.01.015
29. Kano H, Flickinger JC, Nakamura A, et al. How to improve obliteration rates during volume-staged stereotactic radiosurgery for large arteriovenous malformations. *J Neurosurg*. 2018;1(aop):1-8. doi:10.3171/2018.2.JNS172964
30. da Costa L, Wallace MC, ter Brugge KG, O'Kelly C, Willinsky RA, Tymianski M. The Natural History and Predictive Features of Hemorrhage From Brain Arteriovenous Malformations. *Stroke*. 2009;40(1):100-105. doi:10.1161/STROKEAHA.108.524678
31. Berman MF1, Sciacca RR, Pile-Spellman J, Stapf C, Connolly ES Jr, Mohr JP YW. The epidemiology of brain arteriovenous malformations. *Neurosurgery*. 2000;Aug; 47(2):389-96 discusion 297.
32. Gross BA, Du R. Natural history of cerebral arteriovenous malformations: a meta-analysis. *J Neurosurg*. 2013;118(2):437-443. doi:10.3171/2012.10.JNS121280
33. Gross BA, Du R. Rate of re-bleeding of arteriovenous malformations in the first year after rupture. *J Clin Neurosci*. 2012;19(8):1087-1088. doi:10.1016/J.JOCN.2011.12.005

34. Solomon RA CE. ARTERIOVENOUS MALFORMATIONS OF THE BRAIN. *N Engl J Med*. doi:10.1001/archneur.1961.00450180088011

35. Mendelow AD, Gregson BA, Rowan EN, Murray GD, Gholkar A, Mitchell PM. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral haematomas (STICH II): a randomised trial. *Lancet*. 2013;382(9890):397-408. doi:10.1016/S0140-6736(13)60986-1

36. Bervini D, Morgan MK, Ritson EA, Heller G. Surgery for unruptured arteriovenous malformations of the brain is better than conservative management for selected cases: a prospective cohort study. *J Neurosurg*. 2014;121(4):878-890. doi:10.3171/2014.7.JNS132691

37. Ding D, Starke RM, Kano H, et al. Stereotactic radiosurgery for Spetzler-Martin Grade III arteriovenous malformations: an international multicenter study. *J Neurosurg*. 2017;126(3):859-871. doi:10.3171/2016.1.JNS152564

38. Chang SD, Marcellus ML, Marks MP, Levy RP, Do HM, Steinberg GK. Multimodality Treatment of Giant Intracranial Arteriovenous Malformations. *Neurosurgery*. 2003;53(1):1-13. doi:10.1227/01.NEU.0000068700.68238.84

39. Jayaraman M V., Marcellus ML, Do HM, et al. Hemorrhage rate in patients with Spetzler-Martin grades IV and V arteriovenous malformations: Is treatment justified? *Stroke*. 2007;38(2):325-329. doi:10.1161/01.STR.0000254497.24545.de

40. Fahed R, Batista AL, Darsaut TE, et al. The Treatment of Brain Arteriovenous Malformation Study (TOBAS): A preliminary inter- and intra-rater agreement study on patient management. *J Neuroradiol*. 2017;44(4):247-253. doi:10.1016/J.NEURAD.2017.03.003

41. Saatci I, Geyik S, Yavuz K, Cekirge HS. Endovascular treatment of brain

arteriovenous malformations with prolonged intranidal Onyx injection technique: long-term results in 350 consecutive patients with completed endovascular treatment course. *J Neurosurg*. 2011;115(1):78-88. doi:10.3171/2011.2.JNS09830

42. Ding D, Xu Z, Starke RM, et al. Radiosurgery for Cerebral Arteriovenous Malformations with Associated Arterial Aneurysms. *World Neurosurg*. 2016;87:77-90. doi:10.1016/J.WNEU.2015.11.080

43. Ding D, Xu Z, Shih H-H, Starke RM, Yen C-P, Sheehan JP. Stereotactic Radiosurgery for Partially Resected Cerebral Arteriovenous Malformations. *World Neurosurg*. 2016;85:263-272. doi:10.1016/J.WNEU.2015.10.001

44. Grasso G The ARUBA study: what is the evidence? *World Neurosurg* 82: e576, 2014

45. Darsaut TE, Magro E, Gentric J-C, et al. Treatment of Brain AVMs (TOBAS): study protocol for a pragmatic randomized controlled trial. *Trials*. 2015;16(1):497. doi:10.1186/s13063-015-1019-0

46. Ondra SL, Troupp H, George ED, Schwab K. The natural history of symptomatic arteriovenous malformations of the brain: a 24-year follow-up assessment. *J Neurosurg*. 1990;73(3):387-391. doi:10.3171/jns.1990.73.3.0387

47. Reitz M, von Spreckelsen N, Vettorazzi E, et al. Angioarchitectural Risk Factors for Hemorrhage and Clinical Long-Term Outcome in Pediatric Patients with Cerebral Arteriovenous Malformations. *World Neurosurg*. 2016;89:540-551. doi:10.1016/J.WNEU.2016.02.050

48. Starke RM, Kano H, Ding D, et al. Stereotactic radiosurgery for cerebral arteriovenous malformations: evaluation of long-term outcomes in a multicenter cohort. *J Neurosurg*. 2017;126(January):36-44. doi:10.3171/2015.9.JNS151311.

49. Ding D, Ilyas A, Sheehan JP. Contemporary Management of High-Grade Brain

Arteriovenous Malformations. *Neurosurgery*. 2018;65(CN_suppl_1):24-33. doi:10.1093/neuros/nyy107

50. Starke RM, Komotar RJ, Otten ML, et al. Adjuvant Embolization With *N* -Butyl Cyanoacrylate in the Treatment of Cerebral Arteriovenous Malformations. *Stroke*. 2009;40(8):2783-2790. doi:10.1161/STROKEAHA.108.539775

51. Hartmann A, Pile-Spellman J, Stapf C, et al. Risk of Endovascular Treatment of Brain Arteriovenous Malformations. *Stroke*. 2002;33(7):1816-1820. doi:10.1161/01.STR.0000020123.80940.B2

52. Patibandla MR, Ding D, Kano H, et al. Stereotactic radiosurgery for Spetzler-Martin Grade IV and V arteriovenous malformations: an international multicenter study. *J Neurosurg*. 2018;129(2):498-507. doi:10.3171/2017.3.JNS162635

53. Schneider BF, Eberhard DA, Steiner LE. Histopathology of arteriovenous malformations after gamma knife radiosurgery. *J Neurosurg*. 1997;87(3):352-357. doi:10.3171/jns.1997.87.3.0352

54. Stefani MA, Porter PJ, terBrugge KG, Montanera W, Willinsky RA, Wallace MC. Large and Deep Brain Arteriovenous Malformations Are Associated With Risk of Future Hemorrhage. *Stroke*. 2002;33(5):1220-1224. doi:10.1161/01.STR.0000013738.53113.33

55. Chung W-Y, Shiau C-Y, Wu H-M, et al. Staged radiosurgery for extra-large cerebral arteriovenous malformations: method, implementation, and results. *J Neurosurg*. 2008;109(Supplement):65-72. doi:10.3171/JNS/2008/109/12/S11

56. Xiao F, Gorgulho AA, Lin C-S, et al. Treatment of Giant Cerebral Arteriovenous Malformation: Hypofractionated Stereotactic Radiation as the First Stage. *Neurosurgery*. 2010;67(5):1253-1259. doi:10.1227/NEU.0b013e3181efbaef

57. Ren Q, He M, Zeng Y, Liu Z, Liu H, Xu J. Microsurgery for intracranial

arteriovenous malformation: Long-term outcomes in 445 patients. 2017. doi:10.1371/journal.pone.0174325

58. Magro E, Gentric J-C, Batista AL, et al. The Treatment of Brain AVMs Study (TOBAS): an all-inclusive framework to integrate clinical care and research. *J Neurosurg*. 2018;128(6):1823-1829. doi:10.3171/2017.2.JNS162751

Figure legends

Figure 1

ROC curve expressing the model obtained to predict a hemorrhagic event while considering endovascular treatment and vascular eloquence as variables. (AUC=0.775, p=0.002 (95%, CI 0.828-0.919). Overall, embolization treatment and presence of vascular eloquence were variables independently associated with hemorrhagic occurrence. A binary logistic regression analysis showed that eloquent location and vascular eloquence were independent variables for a poor prognosis (OR not determined, CI 95% 0.000; p=0.002; OR 0.084, CI 95%: 0.010-0.737, p=0.005, respectively). Superficial venous drainage was identified as an independent protective factor (OR: 0.061, 95% CI: 0.006-0.653, p=0.006). However, the ROC curve did not show good discrimination (AUC=0.474, p=0.769).

Figure 2

Figure showing the summary of the Cost-effectiveness analysis performed.

Treatment costs included the costs of the planning imaging tests, hospital inpatient stay, treatment procedure, and outpatient follow-up. In the endovascular group, costs included each embolization session. For the SRS group, the costs were obtained from the mean cost of the hypofractionated procedures. For those cases needing embolization of a flow-related aneurysm, the final cost merged by adding up each cost.

The ICER was 53.279 thus suggesting that AVM complete occlusion by embolization would increase the cost approximately of 53.279 USD when compared with SRS.

SRS, Stereotactic Radiosurgery; CEA, cost-effectiveness Analysis; ΔC, incremental cost; ΔE, incremental effectiveness

TABLE 1. Subject Characteristics and Descriptive of AVMs Variables

Variables	Total of cases	Endovascular group	SRS group	P value (p< 0.05)
No. cases	57	26	31	
Demographic				
Age in yr. (mean, range & ±SD)	39 (4-89)	41.4 (± 15.8)	38.45 (±16.0)	0.64
Male (n, %)	30 (52.6)	11 (37.9)	18 (62.1)	0.18
Female (n, %)	27 (47.4)	15 (55.6)	12 (44.4)	
Clinical Variables at presentation				
GCS at presentation (mean ± SD)	13±1.6	13.85 ± 1.1	13.77 ± 1.5	0.44
Incidental (%)	7	11.5	6.4	0.33
Hemorrhage (%)	87.8	32.2	30.8	0.84
I.V. Hemorrhage (%)	14	48.9	51.1	0.71
I.V. Hemorrhage volume <30cc (%)	93	96.1	83.9	0.61
I.V. Hemorrhage volume >30cc (%)	7	3.9	16.1	
Headache (%)	24.6	26.9	22.6	0.76
Blood steal phenomenon (%)	12.3	7.7	16.12	0.43
Seizures at diagnosis (n., %)		34	58.1	0.05*
AVM location				
Deep AVM location * (%)	10.7	6.45	12.9	0.17
Eloquence of location (%)	80.7	65.4	90.3	0.009*
Supratentorial lobar† (%)	98.2	100	96.8	1.00
Ventricular/ Paraventricular (%)	1,7	0	3.2	1.00
Brainstem (%)	0	0	0	.
Cerebellum (%)	1.8	0	3.2	1.00
Angioarchitectonic & location Variables				
Deep venous drainage (%)	64.9	50	77.4	0.038*

Number of feeders (mean ± SD)	3.32 ± 1.9	3.69 (±1.9)	2.65 (±1.8)	0.085
Vascular eloquence (%)	42.1	38.5	45.2	0.53
Diameter of feeders in mm (mean ± SD)	1.79 ± 0.52	1.89 ± 0.53	1.7 ± 0.51	
Perforating artery supply (%)	61.4	42.3	77.4	0.004*
Nidus largest diameter in cm (mean range) or (mean ± SD)	4.99 (3.4-8)	4.89 ±1.12	5.13±1.35	0.56
Nidus volume in cm^3 (mean ± SD)	12.66 ± 11.82	5.36 ± 4.87	18.8 ± 12.5	0.000*
Diffuse (%)	35.1	26.9	35.5	0.44
Aneurysm (%)	19.6	30.7	9.7	0.052
Fistulous components (%)	35.1	73	58	0.30
Number of drainage vein (mean ± SD)	2.46 ± 2	2.23(±0.95)	2.65 (±1.1)	0.154
Presence of venous aneurysm or stenosis (%)	24.5	23	25.8	1.00

For clinical variables at presentation 22.8% of cases presented with two or more symptoms.
* *Deep location refers to the basal ganglia, thalamus, or brainstem;* † *Supratentorial lobar location, frontal, temporal, parietal, or occipital; GCS , Glasgow Coma Scale; I.V., Intraventricular; SD, Standard deviation.*

TABLE 3. Variables showing statistical differences between groups in the present study.

Variable	Embolization (N= 26)	SRS (N= 31)	P value
Seizures at diagnosis (n., %)	9 (34)	18 (58.1)	0.05*
Nidus diameter (cm, SD)	4.9 (±1.12)	5.13(± 1.25)	0.56
Number of veins (mean, SD)	2.23(±0.95)	2.65 (±1.1)	0.154
Number of feeders (mean, SD)	3.69 (±1.9)	2.65 (±1.8)	0.085
Eloquent location (n., %)	17 (65.3)	28 (90.3)	0.009*
Perforating artery supply (n., %)	11 (42.3)	24 (77.4)	0.004*
Deep venous drainage (n., %)	12(46.1)	22 (71)	0.038*

SD, Standard deviation, SRS, stereotactic radiosurgery

TABLE 4. Complications related to treatments between the groups

Variable	Series (N=57)	Embolization (N=26)	SRS (N=31)	P value
Overall complication Rate (n., %)	31 (54.4)	17 (65.4)	14 (45)	0.050
Hemorrhage (n., %)	14 (24.5)	11 (42.3)	3 (10)	0.007
Seizures (n., %)	6 (10.5)	5 (19.2)	1 (3.2)	0.019
Ischemia (n., %)	5 (8.8)	3 (11.5)	2 (6.5)	0.155
Cyst or radio-necrosis (n., %)	2 (3.5)	0	2 (3.5)	0.301
Edema (n., %)	2 (3.5)	1 (3.8)	1 (3.2)	0.157
AVM recanalization (n., %)	2 (3.5)	2 (3.5)	0	0.212
Surgery for complications (n., %)	14 (24.6)	10 (38.4)	4 (13)	0.050

SRS, stereotactic radiosurgery

TABLE 5. Occlusion rate and mRS at follow-up

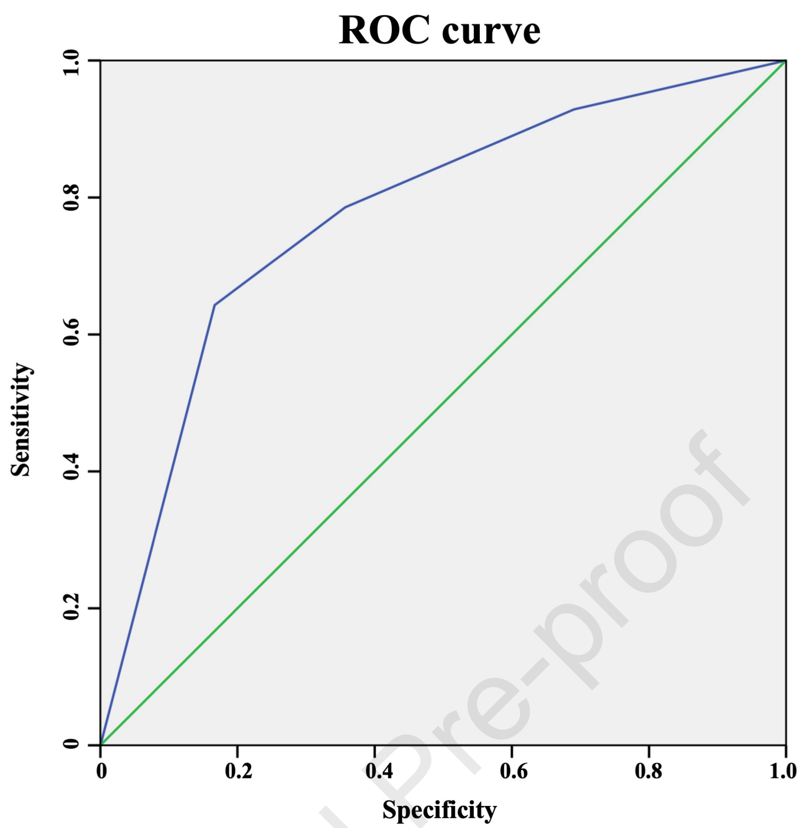
Variable	Series (N= 57)	Embolization (N=26)	SRS (N=31)	P value
Occlusion Rate (n., %)	38 (66.7)	20 (77)	18 (58.1)	0.184
mRS at follow-up				
Favorable (0-2) (%)	89.3	48	52	1.000
Unfavorable (3-6) (%)	10.7	50	50	
Time to occlusion (days, SD)	675,54 (±1239,3)	458,08 (± 675,6)	934,43 (± 1666,9)	0.326

mRS, modified Rankin scale; SD, Standard deviation, SRS, stereotactic radiosurgery

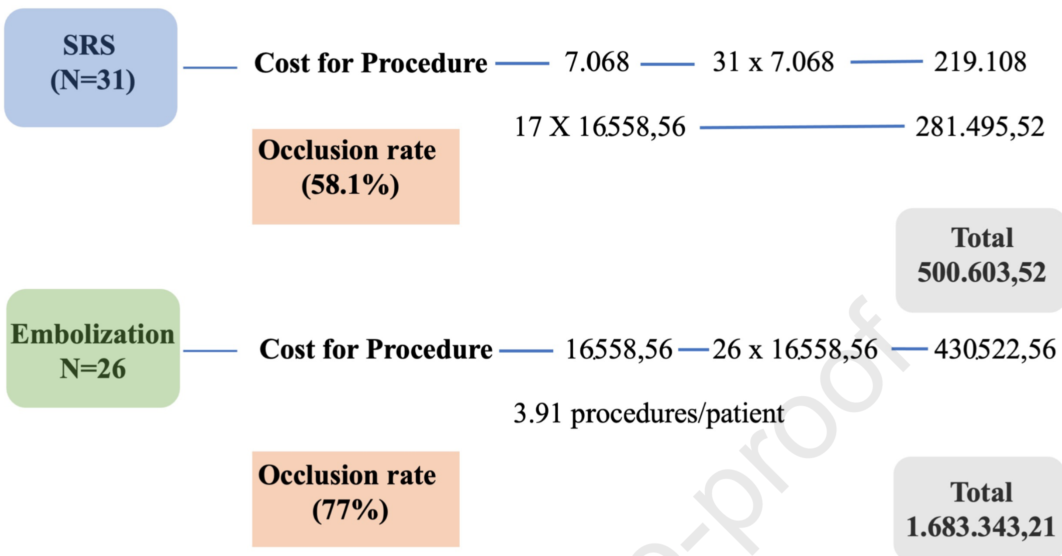
TABLE 2. AVM Location between the treatment groups

		Embolization (n. 26)	SRS (n. 31)	P value
Laterality	Left	11(42,3%)	17 (54.8%)	0.341
	Right	15 (57.7%)	14 (45.2%)	
Eloquent location		18 (69.2%)	28 (90.3%)	0.009
One vs multiple locations	1	21 (80.7%)	25 (80.6%)	1.000
	≥ 2	5 (19.2%)	5 (16.1%)	
Frontal		9 (34.6%)	9 (29%)	0.505
Temporal		10 (38.4%)	8 (25.8%)	0.346
Parieto-occipital		7 (27%)	12 (38.7%)	0.333
Ventricular/ Paraventricular		0	1 (3.2%)	1.000
Cerebellum		0	1 (3.2%)	1.000
Deep Location*		10 (38.4%)	11 (35.5%)	0.172

* *Deep location refers to the basal ganglia, thalamus, or brainstem; SRS, stereotactic radiosurgery*


ROC curve
Sensitivity
0
0.2
0.4
0.6
0.8
1.0
0
0.2
0.4
0.6
0.8
1.0
Specificity

Summary of Cost-effectiveness analysis



Treatment	Cost	Effectiveness	CEA	ΔC	ΔE	ICER
Embolization	1.683.343,21	77%	27550,62	**1182793,69**	**22.2**	**53.279**
SRS	500.603,52	58.1%	12868,98			

Abbreviations :

AVM: arteriovenous malformations
AVMES: Embocure score
CEA: cost-effectiveness analysis
E: eloquent area
HST: hypofractionated stereotactic radiotherapy
ICER: Incremental cost-effectiveness ratio
MRI: Magnetic resonance imagine
mRS: modified Rankin scale
S: size
SM: Spetzler-Martin Scale
SRS: Stereotactic radiosurgery
SVR: stage volume radiosurgery
V: venous drainage

DISCLOSURES

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

SOURCES OF FUNDING

No funding was received for this research.