

Awake Surgery for Arteriovenous Malformations (AVM) in Eloquent Area: Risk and Outcome Analysis in the Most Complete Case-Collection

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Abstract

Background: Artero-venous malformations (AVMs) located in eloquent area are associated with significant risk of neurological deterioration, especially in patients presenting with unruptured AVMs and minimal or no neurological deficits. Awake-surgery allows a better identification of eloquent gyrus, but its feasibility and application in resection of eloquent AVMs is controversial and mostly limited to small case series.

Methods: A total of 31 patients suffering from intracranial AVMs have been operated on in our Department. Patients were stratified into two groups: patients submitted to Asleep Surgery and patients submitted to Awake surgery. We implemented the Awake Group with results from the most complete case series reported in the literature to obtain a complete uni and multivariate analysis of surgical risks and outcome.

Results: Awake craniotomy was performed in 19,35% of the AVMs treated in our centre. Considering the reported cases from all other series published in the literature, we obtained a comparison between the asleep group of 25 patients derived from our series and the awake group of 34 patients. No statistically significant differences were identified regarding the risk of postoperative complications, surgical radicality, presence of residual, and need for adjuvant treatment. Interestingly, however, improvement in performance status was more rapid and effective during follow-up in patients treated with awake surgery compared with asleep surgery.

Conclusions: In contrast to what is commonly believed, applying awake surgery in this type of lesions does not involve increased intra-operative risks, but rather it seems to determine a greater improvement in the outcome of patients from the thirtieth postoperative day. Awake patients allow for more precise brain mapping and superior clinical neurologic monitoring, which facilitates resection by defining the safe margins without an increased risk.

Introduction

Brain arteriovenous malformations (AVMs) consist of a complex tangle of pathologic vessels causing shunting between arteries and veins within the surrounding brain tissue [17].

AVMs located in the motor and language cortex are associated with significant risk of neurological deterioration, especially in patients presenting with unruptured AVMs and minimal or no neurological deficits. These patients are typically managed conservatively or treated radio-surgically, [10] so, the surgical treatment of AVMs located in an eloquent area represents a therapeutic challenge [10, 23].

The Spetzler-Martin grading system (S-M) was proposed to grade and predict morbidity and mortality of operative intervention, where AVMs with S-M Grade I or II have been considered safe for surgical resection [19, 20], however the classification scores 0 or 1 for eloquence of cortex, for its simplicity does not

incorporate the use of functional studies and treatment of AVMs locating in these areas remained controversial.

Eloquence is determined by the normal anatomic position of the eloquent regions [5]. The anatomical landmarks used to localize eloquent cortical regions can be imprecise, and these areas are subject to considerable variability in the location of both motor and language cortex [4]. Also, it is known that congenital cortical lesions such as AVMs may alter functional localization by displacing functional areas to other locations. Therefore, for lesions around or in the eloquent cortex, functional mapping must be performed [1].

Pre-operatively functional imaging can facilitate the localization of the eloquent areas, but recent studies have discussed the usefulness and reliability of functional magnetic resonance imaging (fMRI) in the anatomic localization of language function [5, 19]. There were reports of misleading results and these were associated with the reorganization of eloquent areas in the presence of AVMs [11]. Awake craniotomy for AVM surgery is not a common practice, and this procedure requires an expert team of anaesthetists, neurosurgeons and neuropsychologists who routinely perform awake cranial procedures. Awake surgery of AVMs allows a better identification of eloquent gyrus, but its feasibility and application in resection of eloquent vascular lesions is controversial and mostly limited to small case series.

We evaluated 31 patients who presented to the University of Sapienza of Rome, Italy, Division of Neurosurgery with perisylvian AVMs. Patients were evaluated preoperatively by traditional anatomic studies (MRI and angiogram) as well as fMRI and language testing.

Patients were then stratified into two groups: patients operated on with an Asleep Surgery (Asleep Group) approach and patients operated on with an Awake surgery (Awake group) approach.

With six cases of awake craniotomy for AVM, this challenging and uncommon technique was performed in 19,35% (6/31) of the AVM treated in the study centre. To promote the analysis we considered the reported cases from all other series published in the literature. We found six published series utilizing awake cortical mapping for preservation of function during AVM resection [1, 5, 10, 23, 24]. We implemented the Awake Group with results from the most complete case series reported in the literature to obtain a complete uni and multivariate analysis of surgical risks and outcome.

Materials And Methods

Study Design and Setting

The study was approved by the University of Sapienza of Rome, Policlinico Umberto I Committee on Human Research.

We retrospectively reviewed a consecutive series of patients who underwent surgery for resection of AVMs between January 2016 and January 2020 in the department of Neurosurgery of Policlinico Umberto I of Rome. Data were obtained from an ongoing registry of AVM-patients treated at our

institution. After enrollment, patients were divided into 2 groups according to modality of procedure performed (Group A, Asleep Surgery; Group B, Awake surgery).

Participants and Eligibility

All the patients included in the final cohort meet the following inclusion criteria:

1. Patients with a neuro-radiological diagnosis of unruptured AVMs confirmed by angiographic exam and histopathological analysis.
2. Preoperative KPS scale score >50%.
3. Absence of major neuropsychological deficits preventing the pre and intraoperative testing
4. The estimated target of the surgical procedure was the radical excision of lesion.
5. Patients were included if, in the postoperative period, could undergo in a clinical and radiological follow-up program.
6. Once the residual of the disease was noticed the patient and the relevant imaging were referred again to our attention, to evaluate the feasibility of a second surgery or to address the patient to an adjuvant treatment.
7. Complete and correct data on clinical, radiological, surgical and follow-up records

At admission all patients underwent a general medical, a neurological, and a psychological evaluation. For all the included patients we recorded:-

- Patient-related variables: sex, age, smoking, days of recovery, pre and post-operative KPS, clinical presentation (divided in debut of seizure, focal deficit, headache or incidental, mental dizziness or acute syndrome), antiepileptic prophylaxis and treatment, incidence of post-operative seizures;

- Lesion and surgery-related variables: location and side of the lesions, S-M grade, S-M grade modified by Lawton, presence of perinidal aneurysm, signs of previously hemorrhage, presence of residual after surgery, adjuvant treatment eventually performed.

Clinical informations were obtained by the digital database of our Institution, whereas OS and KPS data were obtained by telephone-interviews. A special focus was centered on the performance status expressed as KPS results in a dichotomy data (> and < 70). In particular it was recorded in three different moments:

1. Before surgery at the time of diagnosis
2. At 30 days after surgery (early post-operative evaluation and
3. At the end of the adjuvant treatment (the moment of the last outpatient evaluation).

We performed a descriptive analysis of all our AVMs cases, partially confirming what was reported in the literature, before focusing on the group analysis implemented to the other series.

Preoperative and Operative Protocol

All the patients included underwent a preoperative CT scanning, brain MRI scan included an high field 3 Tesla volumetric study with the following sequences: T2w, Fluid Attenuated Inversion Recovery (FLAIR), Isotropic Volumetric T1-weighted Magnetization-prepared Rapid Acquisition Gradient Echo (MPRAGE) before and after intravenous administration of paramagnetic contrast agent; diffusion tensor sequences (DTI) with 3D tractography, functional MRI (fMRI) and catheter digital subtraction angiography (DSA).

Patients with AVMs in the language cortex underwent language testing by a neuropsychologist.

Eloquent location was first identified anatomically on MRI and then confirmed by fMRI. Patients with unruptured AVMs directly in the language zone where fMRI had shown activity extremely close (<5mm) or within the nidus were not considered for surgery and referred for other non-surgical options.

All the procedures were performed with an infrared-based Neuronavigator (Brainlab, Kick® Purely Navigation), in a standard neurosurgical theatre, with a standard operative microscope. In the first postoperative day, as routine, the patients underwent a CT scan to exclude major complications and volumetric Brain MRI scan to evaluate the EOR.

General contraindications for awake procedures was uncooperative patients, patients with severe language disabilities (such as frank Wernicke's aphasia), very young patients or patients with significant language barriers. Patient's clinical presentation is also important. Patients presenting with hemorrhage associated with hemiplegia, aphasia or a comatose state may not be good candidates for awake mapping.

Specific relative neurovascular contraindications include large and deep AVMs, posterior fossa cavernomas or AVMs and possibly patients undergoing direct bypasses for Moyamoya disease.

As a standard protocol adopted at our center [2] For Asleep group a standard total intravenous anesthesia protocol with Propofol (1 mg/kg) and Remifentanyl (0.5 mg/kg/min) has been used and maintained until the end of surgery. For Awake group, a standard Full Awake Surgery protocol was routinely performed with the aid of Intraoperative Neuromonitoring realized with use of bi- and monopolar stimulating probes respectively for the cortical and subcortical mapping. During craniotomy and surgical exposure for awake cases, patients were sedated with intravenous agents that included propofol (50-100 mg/□kg/□min) and remifentanyl (0.05-0.2 mg/□kg/□min). Local anesthesia with lidocaine was used for scalp and temporal muscle. Before mapping, sedatives were discontinued and patients were awakened under the care of the anesthesiologist.

In general, it was intraoperatively judged necessary to stop malformation excision when:

1. despite a directly visualized or a Navigation proven remnant, neuromonitoring or intraoperative neuropsychological testing outlined a risk for postoperative motor morbidity,
2. white matter appeared free of tangling vases.

Data sources and Quantitative variables

The presence of residual was determined through a comparison between the MR images and angiography obtained before surgery and the first early angiography after surgery.

In case of residual, we signaled if patient follow a wait-and see follow-up or another surgery/adjutant treatment with radiosurgery.

A close range dedicated neuro-imaging follow-up program was routinely performed in our Institution. This program included:

1. A standard early (maximum 24 hours after surgery) postoperative volumetric brain MRI and angiography.
2. At approximately one month from surgery (25-35 days) a angio-CT scan was repeated for a first step follow-up control;
3. At 6 month/1 year from surgery with CT-Angiography scan;

At every radiological reevaluation we performed a complete outpatient clinical and neurological outpatient re-evaluation.

Size, statistical power of the study and potential source of Bias

The study size is given by selection of the inclusion criteria. As previously stated, we addressed no missing data because incomplete records were an exclusion criterion. A potential source of bias is expected from exiguity of the sample, nevertheless it presents an excellent post hoc statistical estimated power $1-\beta$. 0.87 (for α . 0.05; effect size, 0.74). The sample was analyzed with SPSS v18 (SPSS Inc., Released 2009, PASW Statistics for Windows, Version 18.0, Chicago, Illinois, USA) to outline potential correlations between the investigated variables.

Comparison between nominal variables have been made with Chi² test. Threshold of statistical significance was considered $p < .05$.

Ethical issue

The informed consent was approved by the Institutional Review Board of our Institution. Before surgical procedure, all the patients gave informed written explicit consent after appropriate information. Data reported in the study have been completely anonymized. No treatment randomization has been performed. This study is perfectly consistent with Helsinki declaration of Human Rights in medical Research.

Patient Outcomes

Neurological outcome was assessed using the Karnofsky performance scale (KPS). A single clinical nurse, under the supervision of a neurologist, performed all clinical assessments before any treatment, preoperatively, at 1 month postoperatively, and during the follow-up period. All patients had follow-up data within 1 year of analysis.

AVM-related seizures that interfered with daily activities (working, school, driving, etc) were assigned a score lower than 70.

Research Strategy for Awake series on AVMs

We performed a review of the literature by analyzing all reported cases of AVM treated with awake surgery and mapping with the aim of identifying the clinical features, operative strategies, surgical results, outcome and rate of complications. We adopted PRISMA criteria for clinical research.

Eligibility criteria

Therefore, while screening the literature, we adopted the following inclusion and exclusion criteria:

Meta-analysis, Case series, Clinical study or Clinical image reporting cases of patients who suffered from intracranial AVM for which an awake surgical approach was adopted;

Conversely, we excluded the following:

Cases reported without detailed clinical features of patients; cases reported without description of radiological images, or summaries and book chapters; papers that report other pathologies or in circumstantial mode (out of topic) and papers written in languages other than English.

Information Sources and Search

The English literature was systematically investigated using MEDLINE, the NIH Library, Pubmed and Google Scholar. The last search date was 15 May 2021. The following search terms were used:

Arterio-venous malformation or AVM AND Awake surgery or Awake mapping. Duplicated articles are removed after the first investigation through the libraries.

Results

In a period ranging from January 2015 to January 2020 a total of 31 patients suffering from intracranial MAV have been operated on in our Neurosurgical Departments.

A total of 14 patients were female (45%) and 17 were male (55%) with a 1:2 ratio. The average age of the cohort was 46.3 years \pm 16.7.

In this cohort, MAV favored frontal (14 patients 45.16%) and occipital (6 patients, 19.35%) localization, in general the lesions were more commonly found in the supratentorial compartment (87%). This data is

statistically significant for what frontal involvement is concerned ($p < .001$). No statistically significant preference of side has been outlined.

About smoke habit there is a clear prevalence of smokers in our collection (16 patients, 69.57%).

Looking at the characteristics of the lesions distributing them among the various classes of S-M, the most common type are grade III and grade II AVMs (15 patients, 48.39% and 9 patients, 29.03% respectively); looking instead at the supplemented S-M version proposed by Lawton, most patients had "high risk" characteristics (a score >5 in 20 patients, 64.51%). 8 patients (25.8%) had aneurysms in the context of the AVM in the para-nidal location, identified by angiographic examination, whereas signs of previous hemorrhage identified by MRI examination or observed intra-operatively were present in 21 patients (67.74%).

The most common clinical presentations noted at the first specialist evaluation were the onset of sensory-motor dysfunction (42%) or with seizures (29%).

In a total of 27 cases a radical excision of MAV was achieved without DSA demonstrated residual disease. A total of 29 patients presented a preoperative KPS over 70 before surgery, whereas 26 had the same performance status at the 30th postoperative day reevaluation ($p = .001$) (data reassumed in Table 1).

As previously described, for the comparison between cases treated with awake surgery and cases treated with asleep-surgery, we used the previous case series reported in the literature in which the outcome measures and clinical characteristics were described, implementing them with the awake surgery group.

The search returned a total of 3340 papers. Considering just scientific articles with radiological, surgical studies with cases reported to this initial cohort, accordingly eliminating a total of 3231 abstracts.

The resulting 109 papers are included in our analysis. The aforementioned exclusion criteria were applied. 2 Articles are subsequently excluded after complete revision of the paper. The list of articles are reassumed to the table 1.

We identified 6 final series: Zamorano et. al. 1998 [23] (6 patients), Cannestra et. al. 2004 [5] (5 patients), Gabarros et. al. 2011 [9] (5 patients), Gamble et. al. 2015 [10] (4 patients), Aoun et. al. 2017 [24] (2 patients) and Wang et. al. 2020 [1] (6 patients). The list of articles with description of patients are reassumed in Table 2.

We thus obtained a comparison between the asleep group of 25 patients derived from our series and the awake group of 34 patients.

We compared as variables between the Asleep group and the awake group: age, sex, cigarette smoking, time of hospitalization, clinical onset, side and brain lobe involved, grade S-M assigned, presence of post-surgical residual and complications, and finally Performance status expressed as KPS (greater or less

than 70) preoperative, early postoperative, at 30 days and at the last follow-up (at 1 year) (Data reassumed in Table 3).

By uni and multivariate analysis, no statistically significant differences were identified regarding the risk of postoperative complications, surgical radicality, presence of residual, and need for reoperation or adjuvant treatment. Interestingly, however, improvement in performance status was more rapid and effective during follow-up in patients treated with awake surgery compared with asleep surgery (ANOVA study, sig. = 0.013, fig. 1).

Discussion

AVMs located near or in eloquent areas implies a unique surgical challenge. Neurologic sequelae of the treatment of brain AVMs were extensively investigated, and depending on the S-M grade [19, 20]. The concept of eloquent proximity as a significant factor in surgical morbidity and mortality is supported by several AVM series and there is a strong correlation between the eloquence of the brain tissue adjacent to an AVM and the postoperative development of a new neurological deficit [11, 22]. Predicting postoperative neurologic deficit or even the feasibility of surgery is therefore difficult. In the context of the management of unruptured AVM and the results of the ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations) [18] and the SAIVM (Scottish Audit of Intracranial Vascular Malformations) [21] AVM studies, the phenomenon of cortical reorganization leading to long term neurological recovery may help to justify an upfront risk of AVM intervention. Although the final results of the ARUBA study supported a conservative watch-and-wait strategy, these results were based on 98 actively treated patients, and of these 116 patients, only 18 patients underwent surgical excision alone or in combination with other treatment modalities. So, the ARUBA study was not powered to distinguish among different treatment modalities [3].

The chronic vascular steal caused by AVM can remodel the surrounding cortex, which may alter both its physiology and function. Specifically, AVM located in or adjacent to eloquent brain regions, such as primary motor and somatosensory, speech and language, can result in the translocation of these eloquent functions to neighboring cortical areas. This transference of neurological function from eloquent to non-eloquent brain regions is related to the phenomenon of cortical plasticity [7]

Cortical plasticity may allow for recovery of post-treatment deficits over time, as the functions of eloquent areas, such as motor and language, gradually redistribute to uninjured brain regions.

The widespread adoption of fMRI confirmed the suspicion that translocation of language function to cortex distant from the AVM nidus regularly occurs. Furthermore, this new tool forced clinicians to reconsider anatomically based assumptions about eloquence and thus, actual S-M. fMRI maps utilized in surgical planning are generated from BOLD signals derived from the difference between oxyhemoglobin and deoxyhemoglobin levels of blood by location, thus giving us a proxy for cortical activity in areas where oxygen is being extracted at a higher rate [13]. This may account for inconsistent correlations

between fMRI and intraoperative language mapping that have been reported in tumors, epilepsy, and mixed series including AVMs [11, 16].

Cortical plasticity has been more extensively studied in patients with intrinsic brain tumors and ischemic stroke. Due to the scarcity of AVM relative to the aforementioned diseases, the analyses of cortical plasticity in AVM patients is more challenging to undertake [8].

Awake craniotomy is a well-established technique for epilepsy and brain tumor surgery near the eloquent areas. Since its first introduction by Burchiel in 1989 [4], the evidence of application for Awake surgery for AVM resection is still limited to small case series.

Several common concerns such as the patient's motion during the procedure, the decreased ability to relax the brain when the patient is conscious, the impossibility to use burst suppression essential to several neurovascular procedures increase diffidence in Awake surgery for neurovascular indications. Hence, the metabolic state of the brain cannot be altered in an attempt to protect the brain from ischemia during these surgical procedures [1], but the results of recent prospective studies have largely disproved the notion that shunt-induced reduction in perfusion in the vascular territories surrounding an AVM produces permanent functional deficits [15].

In this study, we showed, with statistical significance, that awake surgery applied to AVM resection does not increase the surgical risk in respect to the standard asleep surgery approach.

The advantages of awake procedures for neurovascular indications may be extrapolated from other neurosurgical pathologies (such brain tumors), due to the exiguity of published data about awake cranial neurovascular procedures and the absence of any randomized trials.

We confirm that the potential benefit of awake surgery for AVMs resection has to balance against the potential intra-operative risks of compromising airway protection, blood pressure control or seizures [23], preservation of neurological function, delineating epileptogenic foci, improving the sensitivity of neuromonitoring, and mitigating the side effects of general anesthesia [1].

Sulcal cortex and subcortical white matter that may be quite eloquent are not accessible until the resection has begun. Therefore, we would argue that maintenance of a wakeful state with language interrogation by subcortical stimulation during AVM resection might provide important feedback to the surgeon, possibly enhancing safety. [11]

Evidence [14] has demonstrated that AVMs in eloquent locations approaching 3cm, and up to 6cm represent a group with higher surgical risks not fully appreciated in neurovascular practice.

Cannestra et al. [5] had proposed a classification of AVM close to the language area suggesting with AVM and language activation are adjacent, awake craniotomy and mapping should be performed [5] to confirm or to identify a high-risk condition. With that, a modified strategy to perform a partial surgical devascularization may be warranted [10].

Like any awake cranial surgery, the success of the procedure is largely dependent on the effectiveness of the anesthesia procedure, patients' cooperation, neuropsychological and neurophysiologic pre-operative and intra-operative assessment.

The technique for awake AVM excision was further advanced with the use of subcortical mapping of the language function [11]. Electrocortical stimulation mapping (ESM) during awake craniotomy has demonstrated great variability in speech center location (Broca's and/or Wernicke's areas). When functional mapping is required, ESM remains the gold standard. Throughout the years, several modalities of non-invasive functional imaging, like fMRIs, PET, and DTI, have augmented but not yet supplanted this more invasive procedure [1] that allows identification of a non-eloquent gyrus for intervention and can potentially facilitate resection with preservation of functions [23].

Further, the assessment of neuropsychological function in AVM patients in the office, in the angiography suite, and on the operating room table is fundamental to select patients and has shown a degree of cerebral redistribution not found or studied as thoroughly to date in any other neurological disease. [15]

Recently it was shown that no differences in neuropsychological testing were found when results were compared according to the nidus location and those patients in whom treatment achieved complete obliteration scored similarly to the normal population, showing that active AVM treatment does not cause deterioration in neuropsychological performance [2,3].

According to the results of our neuropsychological testing, patients with non-obliterated high-grade AVMs (S-M IV–V) scored worse than patients harboring AVMs S-M grade I to III. This finding indicates a possible confirmation of the steal phenomenon, which other authors suggested as the main reason for neuropsychological and neurologic improvement after AVM occlusion [3].

Conclusion

AVMs frequently cause neurological symptoms by affecting the surrounding parenchyma via rupture, development of perinidal gliosis, or shunting of the blood supply [9]. AVMs, have been shown to trigger significant shifts in motor or language function, from their anatomic locations.

Safe microsurgical resection of AVMs in eloquent areas of the dominant cerebral hemisphere can be challenging. Although sophisticated noninvasive functional imaging modalities can facilitate localization of the eloquent area, preoperative functional imaging serves only as a screening test, because there have been reports of inconsistent correlations between the functional imaging and ESM awake mapping [22]. Brain mapping and awake neuro-monitoring should be used during the resection; in contrast to what is commonly believed, applying awake surgery in this type of lesions does not involve increased intra-operative risks, but rather it seems to determine a greater improvement in the outcome of patients from the thirtieth postoperative day. Awake patients allow for more precise brain mapping and superior clinical neurologic monitoring, which facilitates resection by defining the safe margins without an increased risk.

In conclusion, the best intra-operative method for localization of language has been the awake craniotomy with intraoperative electro-cortical stimulation mapping.

Abbreviations

arteriovenous malformations (AVMs), Spetzler-Martin grading system (SM), Electrocortical stimulation mapping (ESM), functional magnetic resonance imaging (fMRI), quality of life (QoL), Karnofski Performance Scale (KPS). digital subtraction angiography (DSA)

Declarations

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Conflict of Interest: We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. We wish to draw the attention of the Editor to the following facts which may be considered as potential conflicts of interest and to significant financial contributions to this work.

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Ethical approval: The authors confirm their adherence to ethical standards and have NO financial disclosures that would be a potential conflict of interest with this publication. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

This article does not contain any studies with animals performed by any of the authors.

Informed consent:

Informed consent was obtained from all individual participants included in the study.

The patient has consented to the submission of this review article to the journal.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order

of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We further confirm that any aspect of the work covered in this manuscript that has involved either experimental animals or human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author and which has been configured to accept email.

Research Data Policy and Data Availability Statements: datasets are actually not deposited in publicly available repositories. The database from Sapienza will be upload on repository IRIS, Sherpa-Romeo.

Author Contributions

Daniele Armocida: writing, sample preparation, presenting results, developed the theory and performed the computations.

Luca D'Angelo: conceived of the presented idea, contributed to the interpretation of the results.

Alessandro Pesce: conceived of the presented idea, performed the analytic calculations;

Antonio Santoro, Alessandro Frati: supervised the project.

All authors discussed the results and commented on the manuscript.

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Tables

Due to technical limitations, tables are only available as a download in the Supplemental Files section.

Figures

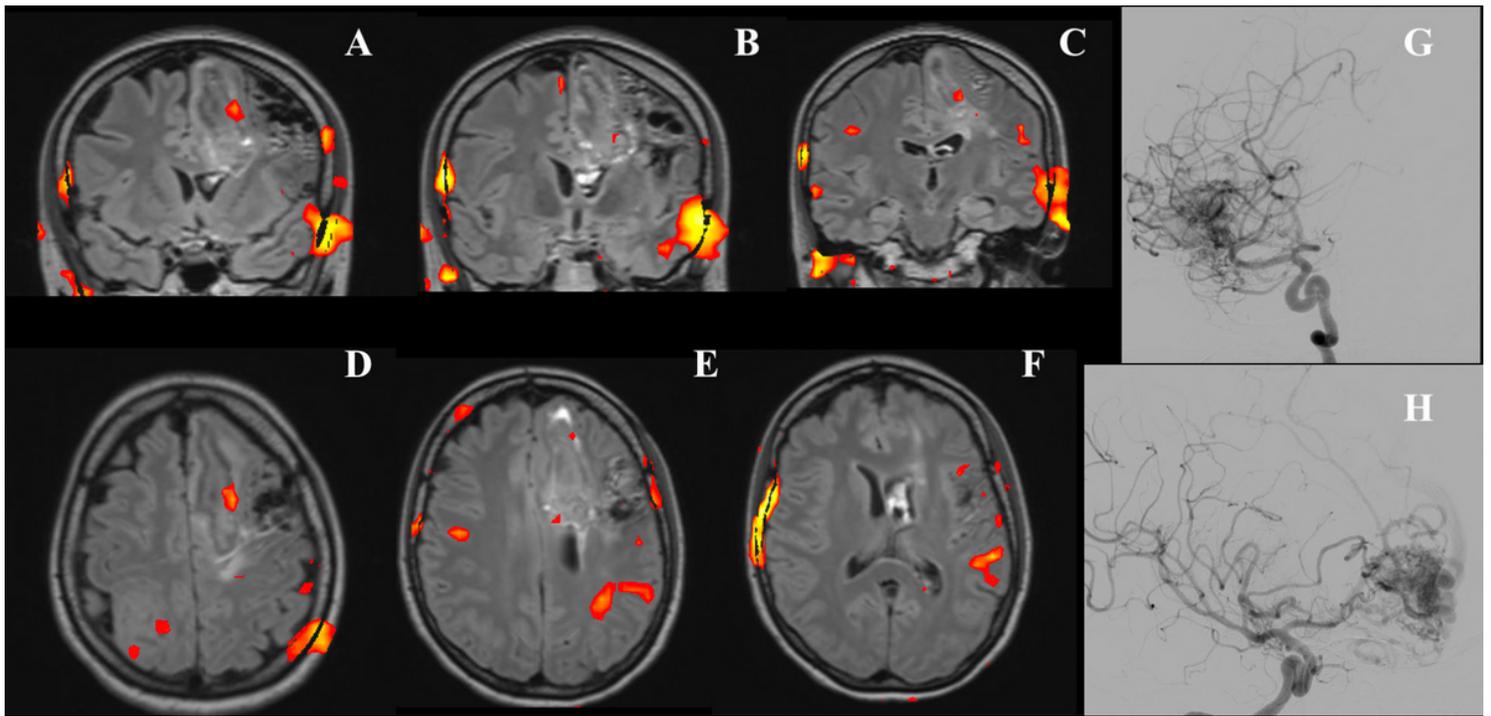


Figure 1

In the functional MRI image of a typical patient with AVM in eloquent area the language areas are commonly distributed in the adjacent cortical areas as visualized in axial (A,B,C) and coronal (D,E,F) sequences. CT-A (G,H) shows the presence of a compact nidus with no signs of recent bleeding.

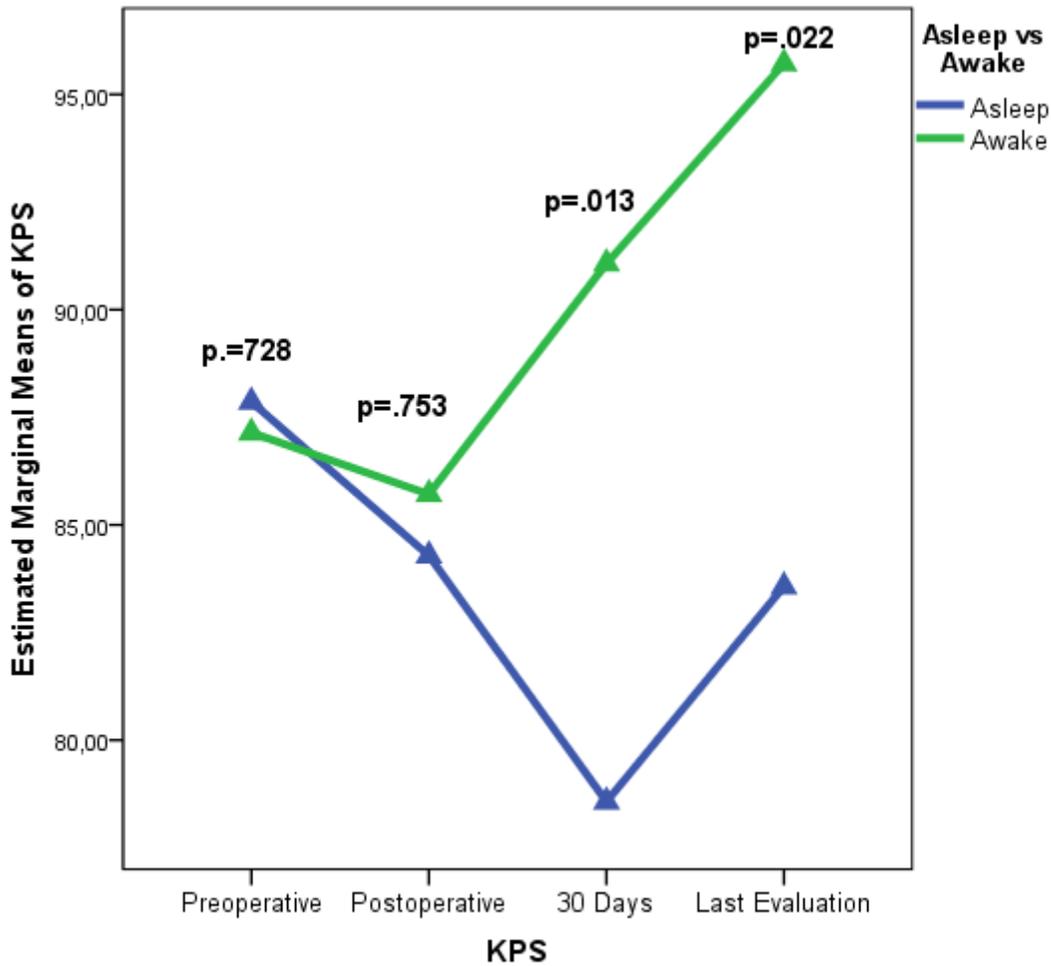


Figure 2

ANOVA graph shows a significant improvement in performance status as measured by KPS after the 30th postoperative day greater in the awake-surgery treated group than in the asleep-surgery treated group.

Supplementary Files

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