

# Management and Surgical Approaches of Brainstem Cavernous Malformations: Our Experience and Literature Review

## Abstract

**Introduction:** Brainstem cavernous malformations (BSCMs) are clusters of dilated sinusoidal channels. Clinical presentation is characterized by focal neurological deficits and/or hemorrhage. The goal of this study is to analyze surgical indications and approaches in a series of patients with BSCM and review pertinent literature and suggest prognostic factors related to the anatomical, clinical, and surgical data collected. **Methods:** We retrospectively reviewed the clinical data of 55 patients with BSCM, treated at three centers, from January 2006 to March 2016. We collected anagraphic data, pre and postoperative neurological status, pre and postradiological images, surgical procedures, and follow-up results. We summarized the anatomical, clinical, and surgical aspects of the lesions and identified two large groups based on the chosen approach: lateral and medial. Clinical and radiological results were then compared. **Results:** The series comprised 55 patients. Hemorrhagic onset was observed in all patients. Suboccipital, retrosigmoid, anterior, subtentorial, subtemporal, transvermian, telovelar, far lateral and trans, and infratentorial approaches were performed. Neurological status improved postoperatively in 34 cases at last follow-up. Five patients showed clinical neurological worsening. Total resection was achieved in 46 cases and, during a mean follow-up of 63.4 months, no recurrence or re-bleeding occurred in those patients. The mean follow-up was 63.9 months. The mean modified Rankin Scale at final follow-up was used to analyze the results and draw our conclusions. **Conclusions:** A reasonable surgical approach, selection, and gentle handling of the surrounding structures are required to prevent impairment of neurologic function and avoid partial resection.

**Keywords:** Brainstem, cavernous malformation, hemorrhagic events, treatment strategy

## Introduction

Cerebral cavernous malformations (CCMs) are proliferative hemorrhagic lesions containing a cluster of vascular sinusoids caverns lined by endothelium and surrounded by gliosis and blood degradation products.<sup>[1-4]</sup> CCMs of the brainstem are particular forms of CMs associated with higher morbidity and mortality rates than other CCMs<sup>[5,6]</sup> due to the proximity of the lesion to critical neural structures and to the complex blood supply in the region.<sup>[7,8]</sup> Brainstem CMs (BSCMs) account for 15%–18% of intracranial CMs with annual re-hemorrhage rates from 5.1% to as high as 30.8%. With regard to the rarity of BSCMs and the potentially devastating consequences of bleeding, different therapeutic modalities have been proposed: conservative, radiosurgery, or surgery. Even though indications for surgery remain controversial, the surgical option

appears the best option for treatment. Our series analyzed 55 patients with BSCMs with the aim of studying the obtained results, viewing them in terms of clinical and radiological outcome considering the surgical approach chosen based on the lesion site, the surgeon's expertise, and data of pertinent literature. Two groups were identified based on the approach performed: lateral and medial.

## Methods

A total of 55 consecutive patients were reviewed retrospectively. The patients were treated between January 2006 and March 2016 in three high-quality centers for the treatment of CMs located in the brainstem or originating from the upper and lower cerebellar peduncles and reaching the brainstem. The follow-up period was from 3 to 154 months (mean: 63.2 months). The patients included in our review had a histopathological diagnosis of CM. Data

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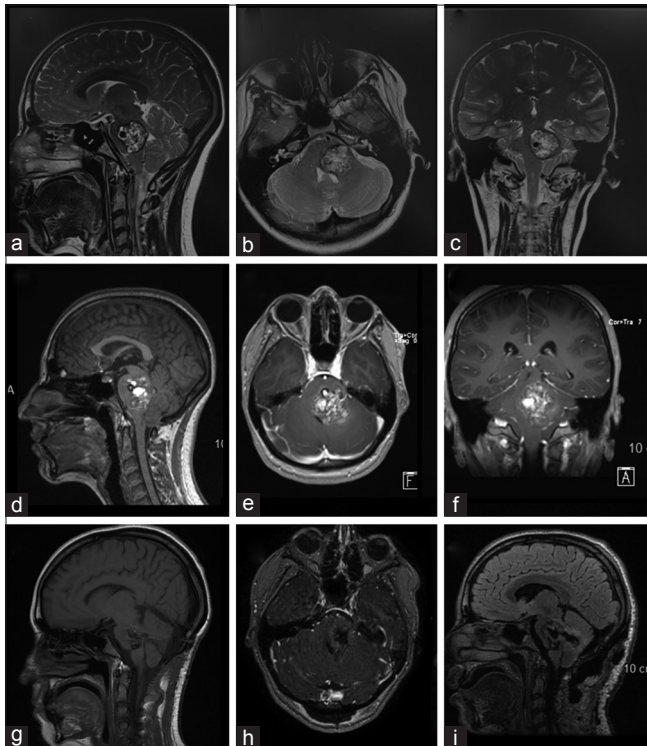
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collected included clinical assessments (on admission, the immediate postoperative period, and at last follow-up), the number of hemorrhagic events, preoperative imaging (magnetic resonance imaging [MRI] including tractography), operative technique (the particularly surgical approach selection), and any complications (re-bleeding and possible additional surgery). We examined early postoperative imaging (MRI within 3 days) and late control (1 year after surgery and every year during follow-up) to define the resection quality (total/subtotal). The location of each BSCM was classified as medullary (10 cases), pontine (22 cases), pontine/mesencephalic (12 cases) and mesencephalic (11 cases), medial (6 medullary, 6 pons, 1 pontomesencephalic, and 8 mesencephalic), and lateral (4 medullary, 16 pons, 11 pontomesencephalic, and 3 mesencephalic). We evaluated the patient's neurological status utilizing the modified Rankin Scale (mRS) score. Demographic, clinical, and surgical data are summarized in Table 1.

Figures 1-4 show some illustrative cases.



**Figure 1:** Case report of a young patient with diplopia (VI nerve paresis). A T2-weighted-magnetic image showed a cavernous malformation with lateral extension in pons-mesencephalon-junction with hemorrhagic signs (a-c). A retrosigmoid approach was proposed, but the patient preferred to delay. After 9 months, the patient presented progressive dysphagia, dysphonia, and ataxia. A new magnetic resonance imaging showed a large cavernous malformation pontomesencephalic (T1-weighted magnetic with gadolinium) (d-f). The patient had V, VI, VIII, and IX severe cranial nerve paresis, VII mild cranial nerve paresis, sensory disturbances, ataxia, and moderate-to-mild disability (modified Rankin Scale score: 2). Intraoperative neurophysiological monitoring was used and a median approach (transvermian) was performed. A postoperative magnetic resonance imaging showed complete removal of brainstem cavernous malformation and initially, the patient was stable, and at last follow-up, presented an improvement of neurological status (g-i)

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. For this type of study, formal consent is not required.

### Surgical technique

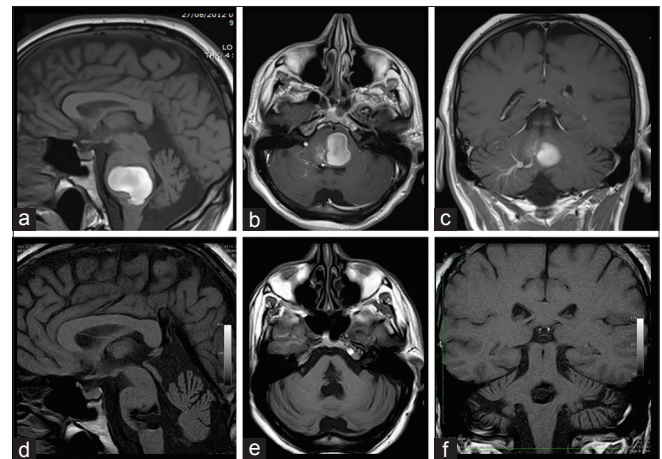
Indications for surgery were as follows:

- Large acute and subacute hemorrhage or large diameter of BSCM
- Severe progressive or worsening of neurological deficits due to repeated hemorrhagic events or enlargement of the BSCM
- More than one hemorrhagic event
- Lesion close to the pial surface, exophytic, or surgically accessible following the preoperative planning.

We did not consider patients for surgery if asymptomatic, or if they had experienced only one hemorrhagic event. We recommend delaying surgery, where possible, for 2–3 weeks, following a symptomatic hemorrhage.

We considered all available approaches to the brainstem to remove CMs. We selected six main approaches based on the shortest trajectories to the BSCM and the senior surgeon's experience. We performed the following approaches in our series:

1. Anterior (orbitozygomatic and pterional) for lateral ventral mesencephalic BSCM
2. Retrosigmoid for ventrolateral pontine or medullary lesions
3. Far lateral for ventral pontine or medullary lesions
4. Suboccipital telovelar for medial dorsal pontine (through the fourth ventricle) and medial dorsal medullary lesions



**Figure 2:** Case report of a middle-aged patient with onset of coma. Preoperative magnetic resonance imaging (a-c) showed a large cavernoma in pons. A medial telovelar approach was performed with intraoperative neurophysiological monitoring (motor, sensitive, and cranial nerve function) and external pacemaker. The patient did not present improvement of neurological status. Postoperative magnetic resonance imaging (d-f) showed complete removal of cavernous malformation

**Table 1: Brainstem cavernous malformations: patient demographics, neurological aspects, lesion location, and modified Rankin Scale score**

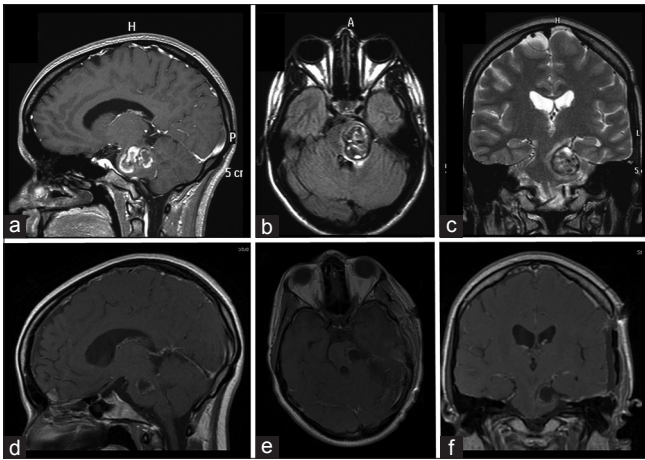
N°	Location	Location	Neurological deficits	Hemorrhagic events	Surgical approach	Removal	Second surgery	Re-bleeding	mRS preoperative	mRS at follow-up	Follow-up (months)
1	Medial	Medulla	Sensory	1	Telovelar	total	No	No	2	0	70
2	Medial	Medulla	Cranial nerve	2	Telovelar	Total	No	No	3	3	50
3	Medial	Medulla	Cranial nerve	1	Telovelar	Total	No	No	4	3	40
4	Medial	Medulla	Cranial nerve	2	Telovelar	Total	No	No	3	2	70
5	Medial	Medulla	Cranial nerve	2	Telovelar	Total	No	No	2	0	40
6	Medial	Medulla	Cranial nerve	2	Telovelar	Total	No	No	2	2	49
7	Lateral	Medulla	Cranial nerve	2	Far lateral	Total	No	No	4	3	69
8	Lateral	Medulla	Cranial nerve	2	Far lateral	Subtotal	No	Yes	3	3	88
9	Lateral	Medulla	Cranial nerve/ataxia	1	Far lateral	Total	No	No	2	1	95
10	Lateral	Medulla	Motor	2	Retrosigmoid	Total	No	No	3	1	10
11	Lateral	Pons	Cranial nerve	7	Far lateral	Subtotal	Yes	Yes	4	2	12
12	Lateral	Pons	Cranial nerve	2	Retrosigmoid	Total	No	No	3	1	87
13	Lateral	Pons	Cranial nerve/sensory	2	Retrosigmoid	Total	No	No	3	3	102
14	Lateral	Pons	Cranial nerve	1	Retrosigmoid	Total	No	No	2	0	97
15	Lateral	Pons	Cranial nerve/sensory	2	Retrosigmoid	Total	No	No	4	2	60
16	Lateral	Pons	Cranial nerve	1	Retrosigmoid	Total	No	No	2	2	107
17	Lateral	Pons	Cranial nerve/motor	2	Retrosigmoid	Total	No	No	1	3	70
18	Lateral	Pons	Cranial nerve	1	Retrosigmoid	Total	No	No	1	2	67
19	Lateral	Pons	Cranial nerve	2	Retrosigmoid	Total	No	No	2	0	55
20	Lateral	Pons	Cranial nerve	2	Retrosigmoid	Subtotal	yes	No	4	3	87
21	Lateral	Pons	Cranial nerve/motor	2	Retrosigmoid	Total	No	No	2	0	69
22	Lateral	Pons	Cranial nerve	2	Retrosigmoid	Subtotal	No	Yes	3	3	76
23	Lateral	Pons	Cranial nerve/motor	2	Retrosigmoid	Total	No	No	3	3	80
24	Lateral	Pons	Cranial nerve	1	Retrosigmoid	Total	No	No	3	3	40
25	Lateral	Pons	Cranial nerve/motor	2	Subtemporal	Total	No	No	3	1	45
26	Lateral	Pons	Motor	2	Retrosigmoid	Total	No	No	2	1	33
27	Medial	Pons	Coma	2	Telovelar	Total	No	No	4	4	35
28	Medial	Pons	Cranial nerve/motor	2	Telovelar	Subtotal	No	Yes	3	4	37
29	Medial	Pons	Cranial nerve/sensory	1	Transvermian	Total	No	No	3	1	15
30	Medial	Pons	Cranial nerve/motor	2	Transvermian	Total	No	No	3	1	40
31	Medial	Pons	Cranial nerve	2	Telovelar	Total	No	No	2	2	90
32	Medial	Pons	Cranial nerve	2	Transvermian	Subtotal	No	No	2	2	72
33	Lateral	Pontomesencephalic	Cranial nerve/motor	1	Subtemporal	Total	No	No	3	0	42
34	Lateral	Pontomesencephalic	Cranial nerve sensory/motor	1	Subtemporal	Total	No	No	3	1	154
35	Lateral	Pontomesencephalic	Motor/sensory	1	Subtemporal	Total	No	No	3	1	62
36	Lateral	Pontomesencephalic	Cranial nerve/sensory/ataxia	1	Subtemporal	Total	No	No	3	0	57
37	Lateral	Pontomesencephalic	Motor	1	Subtemporal	Total	No	No	3	1	86
38	Lateral	Pontomesencephalic	Motor/sensory	1	Subtemporal	Total	No	No	3	1	58

Contd...

Table 1: Contd...

N°	Location	Location	Neurological deficits	Hemorrhagic events	Surgical approach	Removal	Second surgery	Re-bleeding	mRS preoperative	mRS at follow-up	Follow-up (months)
39	Lateral	Pontomesencephalic	Cranial nerve/motor/sensory	2	Subtemporal	Total	No	No	3	1	110
40	Lateral	Pontomesencephalic	Motor/sensory	2	Subtemporal	Total	No	No	3	1	72
41	Lateral	Pontomesencephalic	Motor	1	Subtemporal	Total	No	No	3	0	12
42	Lateral	Pontomesencephalic	Motor/ataxia	1	Retrosigmoid	Total	No	No	2	0	34
43	Lateral	Pontomesencephalic	Ataxia	1	Retrosigmoid	Total	No	No	2	1	24
44	Medial	Pontomesencephalic	Cranial nerve/motor	4	Transvermian	Total	No	No	2	2	1
45	Lateral	Mesencephalic	Cranial nerve	1	Anterior	Subtotal	No	No	3	3	18
46	Lateral	Mesencephalic	Cranial nerve/sensory	5	Subtemporal	Total	No	No	3	2	15
47	Lateral	Mesencephalic	Motor	2	Anterior	Subtotal	Yes	No	3	2	88
48	Medial	Mesencephalic	Cranial nerve/motor	2	Transstentorial	Total	No	No	2	2	103
49	Medial	Mesencephalic	Ataxia	2	Transstentorial	Total	No	No	2	0	123
50	Medial	Mesencephalic	Cranial nerve/ataxia	1	Transstentorial	Total	No	No	1	0	79
51	Medial	Mesencephalic	Motor	1	Infratentorial	Total	No	No	2	4	48
52	Medial	Mesencephalic	Cranial nerve/motor	2	Infratentorial	Total	No	No	4	3	110
53	Medial	Mesencephalic	Cranial nerve	1	Infratentorial	Total	No	No	1	1	76
54	Medial	Mesencephalic	Cranial nerve/sensory	1	Transstentorial	Total	No	No	2	3	102
55	Medial	Mesencephalic	NNCC/ataxia	3	Telovelar	Subtotal	No	No	3	3	46

MRS – Modified Rankin Scale; NNCC – Cranial nerves



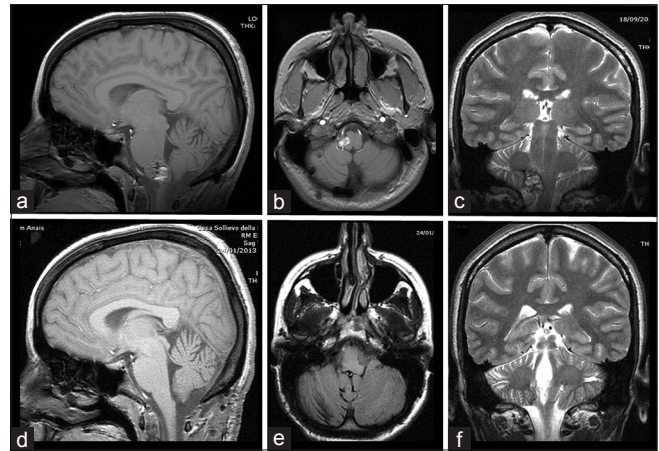
**Figure 3:** Case report of a middle-aged patient with ataxia, right hemiplegia, and sensory disturbance. Preoperative magnetic resonance imaging indicated a left pontomesencephalic cavernous malformation. A subtemporal approach was performed with intraoperative neurophysiological monitoring. Postoperative magnetic resonance imaging showed complete removal and no left temporal lobe damage. Neurological status was completely recovered at 30 days

5. Supracerebellar infratentorial for medial dorsal mesencephalic lesions
6. Subtemporal approaches for lateral pontine, ponto-mesencephalic, and mesencephalic lesions.

In 15 cases, neuronavigation and image guidance provided real-time anatomic localization of the BSCM and its relationship to eloquent tissues, particularly for lesions that did not reach the surface. A cardiac pacemaker was used in 13 cases. Neurophysiologic monitoring, including somatosensory and motor-evoked potentials, was used in all cases. Moreover, neurophysiologic mapping was used to check cranial nerve response. The aim of this surgery was to plan the most appropriate approach, minimize possible surgical complications, and choose the safest entry route.

The relationship between the cavernoma and pial or ependymal surface of the brainstem helps to define the choice of surgical approach. The supra- and infra-facial triangles at the floor of the fourth ventricle, the lateral mesencephalic sulcus, the peritrigeminal area, and the inferior olivary nucleus are described as entry zones<sup>[9,10]</sup> which allow an anatomical route to preserve neurovascular structures.

Since all of our cases were localized lower than 3 mm below the pial surface, we did not have to select a real safe entry zone because the thin layer did not involve any neurovascular structures, so the lesion itself dictated the entry point. The microsurgical technique performed in all of our cases was the 2-point rule, introduced by Brown *et al.*,<sup>[11]</sup> to choose the optimal angle of entry for each lesion already planned with the aid of high-resolution preoperative images. All patients underwent computed tomography scan postoperatively. Patients were maintained on mechanical ventilation in the Intensive Care Unit for a minimum of 24 h following the surgical procedure.



**Figure 4:** Case report of a 20-year-old patient with dysphagia, VII nerve palsy, and ataxia. Preoperative magnetic resonance imaging (a-c) showed a small medullary cavernous malformation. Intraoperative external pacemaker and neurophysiological monitoring were used. A far-lateral approach was applied and complete removal and resolution of symptoms were obtained

### Statistical analysis

The data values are summarized as median, mean, and range for continuous variables and as frequency and percentage for categorical variables. Statistical analyses of categorical variables were carried out using the Fisher's exact tests for linear association as appropriate and nonparametric tests (median values and ranges as well as numbers and percentages).  $P \leq 0.05$  was considered statistically significant. We compared the mRS score for each surgical approach used and formed them into two main subgroups according to lateral and medial locations of BSCM. When the  $\Delta$ mRS was higher than 0, it indicated neurological improvement;  $\Delta$ mRS = 0 means stability of neurological status and  $\Delta$ mRS < 0 means worsening of neurological status.

### Results

Fifty-five patients (23 males and 32 females) were included in our series. The mean age was 40 years (range: 16–70 years). The principal localizations were medulla in 18% of cases (10 patients), pons in 40% (22 patients), ponto-mesencephalic junction in 21% (12 patients), and mesencephalon in 20% (11 patients).

The onset of signs and symptoms included cranial deficits in 74.5% of cases, motor deficits in 40% of cases, sensitive deficits in 22% of cases, ataxia or dysmetria in 12% of cases, and an altered level of consciousness in 1.8% of cases. The main subjective symptoms were headache, dizziness, nausea, and/or vomiting.

In our series, 22 patients complained of 1 hemorrhagic event. Surgical procedure was considered for these patients when there was a complaint of neurological deficit and when the size of the CM, or hemorrhage, was significant. Two hemorrhagic events occurred for 29 patients, while >2 events occurred for the remaining 4 cases

(3, 4, 5, and 7, respectively). A surgical procedure was selected for those cases, in accordance with our indications.

Clinical, demographic, and surgical data relative to location are summarized in Table 2.

A gross total resection was achieved in 46 patients (83.6%). The most faceable sites to reach this result were the ponto-mesencephalic-junction (100%) and the medullary (90%).

Subtotal resection was achieved in nine cases. Three patients out of the nine underwent a second surgery: 1 patient to remove an important residual lesion through a surgical access, 1 patient because of the persistence of preoperative symptoms, and 1 patient because of a second hemorrhagic event. We observed an improvement in the neurological status for all patients who underwent an additional surgical procedure. Six patients of the nine with residual CM were not considered for a second surgery due to the small size of the residual lesion or because they were asymptomatic. Three of these did not re-bleed at last follow-up and did not show any neurological change. The remaining three patients re-bleed: one showed worsening in neurological status, while the two remained stable.

In summary, we observed improvement in the subtotal removal group (nine patients) of neurological status and mRs score at last follow-up in three patients who underwent an additional surgical procedure. The five patients who were not re-operated on remained stable at follow-up: two notwithstanding re-bleeding and one patient worsened after re-bleeding and conservative treatment.

The approaches were chosen depending on the localization of the lesion.

The BSCMs were medial in 21 patients, and the approaches selected were telovelar, transtentorial, infratentorial, and

transvermian. In 34 cases, the lesion was lateral and the approaches performed were anterior, retrosigmoid, far-lateral, and subtemporal. We observed a neurological improvement in 70% of patients who underwent lateral approach and a neurological worsening in 8.8% of cases. Regarding the medial approaches, we observed neurological improvement in 47% of cases and neurological worsening in 14% of cases.

We compared lateral and medial approaches to the BSCMs in relation to the mRS score (postoperative and at clinical follow-up) [Table 3].

Significant statistical data were obtained with  $P = 0.0086$ , which indicates that the lateral approach, in our series, is associated with a better neurological and clinical outcome.

At the last follow-up (3–154 months), we observed an improvement in the mRS score in 34 cases, a decline in the neurological status in 5 patients, while 16 patients remained stable.

## Discussion

The correct management of BSCM requires careful knowledge of the epidemiology, natural history, and clinical presentation. Patients affected by BSCMs are usually symptomatic, mainly because of hemorrhagic event or due to the size of the CM.<sup>[5]</sup>

Despite our increasing knowledge regarding natural history, there is currently no available treatment algorithm for cavernomas. Three treatment modalities (observation, microsurgery, and radiosurgery) have been discussed in the literature, but their indication criteria are yet to be defined. Frischer *et al.*<sup>[12]</sup> reported on a treatment model in which the microsurgical resection is suggested for symptomatic lesions with suitable operative corridors, gamma knife

**Table 2: Clinical, demographic, and surgical 10.325 data according to location in brainstem of cavernous malformations**

	Mesencephalon	Pontomesencephalic junction	Pons	Medulla
Total	11 (20)	12 (21)	22 (40)	10 (18)
Age	43.5	32.5	41.8	41.4
Sex ratio (female:male)	4:7	11:1	12:10	5:5
>1 hemorrhagic event	6 (54.5)	3 (25)	17 (77)	7 (70)
Total removal	8 (72.7)	12 (100)	17 (77)	9 (90)
Second surgery	3 (27)	0	2 (9)	0
Re-bleeding	0	0	3 (13.6)	1 (10)
Surgical approach				
Telovelar	1 (9)	-	3 (13.6)	6 (60)
Transtentorial	4 (36.3)	-	-	-
Infratentorial	3 (25)	-	-	-
Subtemporal	1 (9)	9 (75)	1 (4.5)	-
Anterior	2 (18.1)	-	-	-
Transvermian	-	1 (8.3)	3 (13.6)	-
Retrosigmoid	-	2 (16.6)	14 (63.6)	1 (10)
Far lateral	-	-	1 (4.5)	3 (30)

**Table 3: Statistical data of two subgroups: lateral and medial location of brainstem cavernous malformations**

Localization in brainstem	Number of patients	Minimum ( $\Delta$ mRS)	Maximum ( $\Delta$ mRS)	Mean $\Delta$ mRS
Lateral	33	-2	3	2
Medial	21	-2	2	0
Total	54	-2	3	1

Statistical data based on  $\Delta$ mRS. A result  $>0$  corresponds to a neurological improvement; a  $\Delta$ mRS=0 means stability of the neurological status and a neurological worsening corresponds to a  $\Delta$ mRS $<0$ . MRS – Modified Rankin Scale

radiosurgery for surgically high-risk deep-seated lesions,<sup>[13]</sup> and conservative management of asymptomatic lesions. In our opinion, as Almefty and Spetzler<sup>[5]</sup> reported, there is no available literature on the use of gamma knife radiosurgery for CMs. Hence, we recommend conservative management for all the lesions considered unsuitable for resection. With regard to microsurgical treatment, one of the most important aspects related to the natural history of BSCMs is their re-hemorrhagic rate following an initial hemorrhage. Contrasting data are reported in the literature regarding re-hemorrhagic rates. In 2010, Abla *et al.* reported a series of 260 patients with a rate of re-hemorrhage  $>30\%$ .<sup>[14]</sup> In 2015, Starke reported a re-hemorrhagic rate for BSCMs which varied from 5% to 21.5%.<sup>[15]</sup> In 2016, Walcot *et al.* observed an estimated 5-year recurrent hemorrhagic risk of 30.8%, with a 50.7% risk of developing either a recurrent hemorrhage or a new neurological deficit unrelated to hemorrhage.<sup>[8]</sup>

Of the 55 patients reviewed, the bleeding rate in female patients was higher than that for male patients (female-to-male ratio – 32:23), probably indicating a hormonal effect on the cavernoma.<sup>[16]</sup> We observed a single hemorrhagic event in more females than males (female/male ratio – 14:8), while multiple hemorrhagic events were found equally in both sexes (female/male ratio – 18:15). These data suggest the same chance of re-hemorrhage rate after an initial hemorrhage despite a predominant female population with a single hemorrhagic event. The frequency and number of hemorrhages are essential in the decision-making process. In fact, re-hemorrhaging of a BSCM increases the rate and severity of neurologic deficits or the worsening of preexisting symptoms and occasionally, it is the cause of death. The hemorrhage rate should be compared with clinical symptoms and signs when deciding upon surgical strategy. The surgical procedure should be scheduled as soon as possible so as to prevent re-bleeding and reduce perioperative risks.

Bertalanffy *et al.*<sup>[17]</sup> reported that symptomatic lesions on the pial or ependymal surface can be considered for resection, while asymptomatic lesions should be managed conservatively. Petr and Lanzino<sup>[18]</sup> agree with the literature in considering surgery for patients who have experienced

at least two symptomatic bleeds and for lesions that come close to the pial surface. In 2015, Horne *et al.* made a very important contribution to our knowledge of the natural history of CMs<sup>[19]</sup> reporting on a large meta-analysis providing strong evidence for long-held suspicions that brainstem location and hemorrhagic lesions portend a more aggressive clinical course.

In our series, a surgical procedure was performed after the careful analysis of each single case, based on size, location, multiple hemorrhagic events, and consequently signs of worsening of neurological status.

In 1999, the Barrow Neurological Institute reported on a consecutive series of 100 patients with BSCMs. The authors suggest that in symptomatic hemorrhage patients a standard skull base approach should be performed when lesion reaches the pial surface. In this series, the standard skull base approaches were practiced in 86% of the cases.<sup>[2]</sup> Nearly 87% of the patients were stable or better at follow-up, 10% were worse, and 4% died. Similarly, in our series, 29% of patients remained stable, 62% were better at the follow-up, 9% were worse, and none died. We agree with the literature that CMs localized on the surface of the brainstem are more easily approachable. In our series, we did not observe a distance between ependymal surface and CM  $>3$  mm that offered a direct and safe entry route due to a thin parenchymal layer. When critical neural structures are sparse and perforating arteries are involved along surgical corridors, a safe entry zone has to be used, as well described in the literature.<sup>[9,10,14,20]</sup> We selected skull base approaches in 62% of the cases, our analysis compared lateral and medial approaches in terms of outcome. A statistical significant value evidenced that the lateral approaches are associated with a better outcome.

Another controversial aspect involving BSCMs is an indication of a second surgical procedure. In 2003, Wang *et al.*<sup>[21]</sup> reported a series of 137 cases in which, at follow-up, a total cavernoma resection was obtained in 96% of cases and a subtotal removal was achieved in 4%. Moreover, the rate of re-bleeding was 2.3% and three patients underwent a secondary operation. The authors suggested that the high bleeding and re-bleeding rate of BSCMs would have resulted from its biologic uniqueness.

In our series, a total resection was achieved for 46 patients (83.6%), a subtotal removal in 9 cases (17.4%), and the re-hemorrhage rate was 7% at follow-up (48 months). We considered a second operation for four patients. Surgical criteria to second treatment were relevant residual lesion, persistence of preoperative symptoms, and re-bleeding. We were conservative in nonsymptomatic and nonhemorrhagic cavernomas or residual in brainstem, poor clinical status, and when the risks of surgery outweighed the benefits. We analyzed the number of hemorrhagic events and the timing (days) from last bleeding to surgery, both resulted similar to data reported in the literature [Table 4].

**Table 4: Relation between hemorrhagic event and timing (days) from last bleeding to surgery**

	Mesencephalon	Pontomesencephalic junction	Pons	Medulla
several hemorrhagic events	6	3	17	7
Time from last bleeding to surgery±SE	40±6	78±9	55±5	35±6

SE – Standard error

Garcia *et al.* (2015)<sup>[22]</sup> highlighted that the number of BSCM hemorrhages is beyond the surgeon's control as well as being difficult to assess, whereas the timing of surgery relative to hemorrhage can be arranged by the neurosurgeon.

Numerous technological advances have been carried out over the past two decades to reduce the intraoperative risks in this kind of surgery.<sup>[23-25]</sup> Intraoperatively, we utilized the navigation system with fusion of preoperative magnetic resonance, neurophysiological monitoring, and, in selected cases, a pacemaker was placed preoperatively.

Limit: This is a retrospective study, notwithstanding our results are now confirmed by the new cases.

## Conclusions

As our analysis suggests, we recommend preference for a lateral approach where possible to reach BSCM. Moreover, according to evidence for a better outcome and lower re-bleeding risk, we suggest performing a second surgical procedure when a residual BSCM is present. However, each patient needs to be evaluated individually, in view of their clinical history, lesion's location, and the surgeon's technical expertise.

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## Conflicts of interest

There are no conflicts of interest.

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