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Brainstem cavernomas malformations. A systematic review and metanalysis on management, concepts and outcomes

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ABSTRACT

Background: Brainstem cavernous malformations (BCM) are supratentorially located vascular structures that damage the central nervous system. The rarest forms of these malformations are found in the brainstem and cerebellum, associated with venous abnormalities that appear suddenly. The aim of this study is to demonstrate the importance of proper anatomical management of cavernous malformations of the brainstem and the optimal resection, whether endoscopic endonasal, microsurgical, suboccipital approaches, or craniotomy, in terms of neurological postoperative results.

Material and methods: The search was exhaustive; it spanned several databases, including ScienceDirect and PubMed/MEDLINE, and was conducted using the PRISMA guidelines, R software for systematic reviews and meta-analyses, and Excel. Search terms included "Brainstem Cavernoma Malformations" along with terms specifying surgical techniques, brainstem or brainstem rehabilitation methods, and associated pathologies. Only studies published in English up to June 2025 were included.

Results: In this systematic review and meta-analysis, we included a total of 1319 patients, of which GTR, N = 269 (20.3%), and STR, N = 14 (1%), were total. Table 1-3, while in Table 1-Figure 2, we included N = 931 (70.5%) patients, GTR, N = 207 (15.6%), and one STR, N = 9 (0.6%).

Conclusion: This study shows that microsurgical resection of cavernous malformations of the brainstem is not only a complex issue in terms of the treatment of this pathology. Even so, endonasal endoscopy is gaining more and more strength, since 80% of resections, even with complications, have been very effective in terms of rehabilitation and postoperative follow-up.

Keywords
brainstem,
cavernomas,
malformations,
stereotactic radiosurgery,
endoscopy,
microsurgery

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INTRODUCTION

Brainstem cavernous malformations (BCM) are supratentorially located vascular structures that damage the central nervous system. The rarest forms of these malformations are found in the brainstem and cerebellum, associated with venous abnormalities that appear suddenly in form families. The symptoms of MCB may be accompanied by headaches, seizures, and sensory and motor disturbances, as well as focal neurological deficits, depending on the anatomical location of the lesion. [1].

BCM has an incidence of 0.5% to 10% of all intracranial vascular malformations in the population. It also has a brainstem prevalence ranging from 4% to 35%. [2]. McCormick recognized that BCMs are a type of microhemorrhagic malformation that causes thrombosis and can be recurrent and that they are composed of hemosiderin deposits and gliosis. Therefore, BCMs are arteriovenous malformations with developmental venous anomalies and capillary telangiectasias, which he emphasized in mid-1966. As a lesion with slow flow and low pressure, their risk of rupture will be lower than in other similar vascular pathologies or malformations. [3].

Brainstem MCLs are considered inoperable, which is determined through patient selection that involves intraoperative guidance during surgical exposures, magnetic resonance imaging guidance during surgery, or MRI tractography, along with neurophysiological monitoring. [4]. Microsurgical resection is the optimal treatment for brainstem MCBs; although it is a strategic treatment, it remains controversial, as it was first reported as a brainstem treatment modality. However, with modern advances in neuroanesthesia, intraoperative , imaging techniques, and postoperative care, stereotactic radiosurgery has emerged as a surgical alternative for brainstem MCBs, following reports of successful outcomes. [5]. The aim of this study is to demonstrate the importance of proper anatomical management of cavernous malformations of the brainstem and the optimal resection, whether endoscopic endonasal, microsurgical, suboccipital approaches, or craniotomy, in terms of neurological postoperative results.

MATERIAL AND METHODS

A systematic review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The review focused on surgical outcomes and approaches, management, and treatment modalities related to The search was exhaustive; it spanned several databases, including ScienceDirect and PubMed/MEDLINE, and was conducted using the PRISMA guidelines, R software for systematic reviews and meta-analyses, and Excel. PROSPERO ID: 1088691. Search terms included "Brainstem Cavernoma Malformations" along with terms specifying surgical techniques, brainstem or brainstem rehabilitation methods, and associated pathologies. Only studies published in English up to June 2025 were included.

The PICO (Population, Intervention, Comparison, Outcome) framework was used to define the study population, focusing on patients aged 1 to 61-85 years with BCM (Figure 1). Search Strategy and MeSH Terms

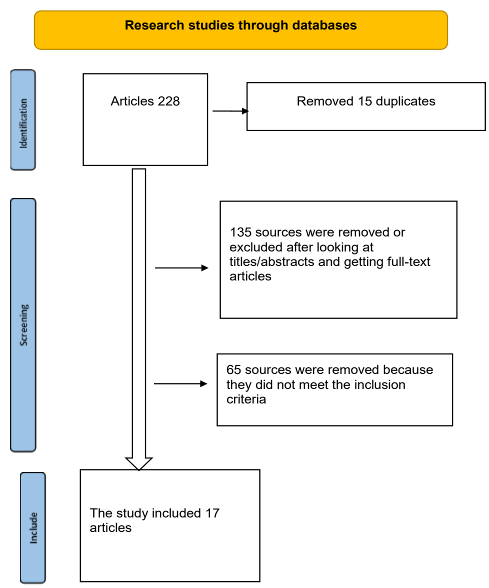

Figure 1. PRISMA Flowchart for Brainstem Cavernomas malformations Study.

The search strategy included MeSH terms (Medical Subject Headings) related to brainstem compression injuries or brain dislocation or herniation:

- "Brainstem Cavernomas malformations/cerebrospinal fluid"[Mesh]
- "Brainstem Cavernomas malformationss/complications"[Mesh]
- "Brainstem Cavernomas malformations/diagnosis"[Mesh]
- "Brainstem Cavernomas malformations/diagnostic imaging"[Mesh]
- "Brainstem Cavernomas malformations/diet therapy"[Mesh]

- "Brainstem Cavernomas malformations/drug therapy"[Mesh]
- "Brainstem Cavernomas malformations/epidemiology"[Mesh]
- "Brainstem Cavernomas malformations/etiology"[Mesh]
- "Brainstem Cavernomas malformations/mortality"[Mesh]
- "Brainstem Cavernomas malformations/pathology"[Mesh]
- "Brainstem Cavernomas malformationsphysiopathology"[Mesh]
- "Brainstem Cavernomas malformations/prevention and control"[Mesh]
- "Brainstem Cavernomas malformations/psychology"[Mesh]
- "Brainstem Cavernomas malformations/radiotherapy"[Mesh]
- "Brainstem Cavernomas malformations/rehabilitation"[Mesh]
- "Brainstem Cavernomas malformations/surgery"[Mesh]
- "Brainstem Cavernomas malformations/therapy"[Mesh]

Keywords

Additional keywords included "Brainstem," "Cavernoma," "Malformation," "Hemiparesis," "Stereotactic surgery," "Microsurgery," "Posterior cranial fossa," "Surgical Approaches," and "Endoscopy."

Inclusion Criteria

- Age range: 1 to 61-85 years.
- Approaches to and management of brainstem cavernous malformations.
- Use of magnetic resonance imaging strategies for the localization and removal of brainstem cavernous malformations.
- Postoperative MRI and CT scans, looking for bleeding or recurrence.
- Postoperative neurological outcomes: paraplegia, dysphagia, hemiparesis, or quadriplegia.

Exclusion Criteria

Discarded patients, misdiagnosed by imaging, who turn out not to be cavernous malformations but rather metastatic tumors, calcified lesions, or cerebrovascular vasculitis.

Pathologies that mimic brainstem cavernous malformations, such as capillary telangiectasias and arteriovenous malformations.

Data Collection

We collected data from the included studies covering various aspects of brainstem cavernous malformations (BCMs), including diagnosis, management, and removal of BCMs. Factors influencing brainstem or cerebral hemorrhage were examined, with analysis of paraplegia, hemiparesis, or quadriplegia, along with details on the types of surgical or conservative techniques, such as early decompression after craniectomy or midline suboccipital or far lateral suboccipital approaches, and conservative management of postoperative pain in general. Rehabilitation, recovery, and neurological follow-up techniques for postoperative sequelae were also reviewed.

Data Extraction and Analysis

Data extraction was performed using standard systems and a rigorous analysis of manuscripts, articles, and relevant research materials. We collected all detailed information on the study concept, including demographic characteristics, interventions, control parameters in comparative studies, authorship, as well as the year of publication and study design.

Risk of bias in individual studies.

We used the Kaplan survival methodology and the pathways for total and subtotal clearance of brainstem cavernous malformations. We assessed the risk of bias in terms of management, BCM, and the development of postoperative microbleeds, taking into account incomplete clearance. T the limitation to cavernous malformations in the brainstem and the type of approach being evaluated. We considered the etiology to surgical treatment.

Analytical Statistics

R as summary statistics for each relevant incidence. The weighted mean difference (OR) with a 95% confidence interval (CI) was used to determine the outcomes of greatest interest to the study. Individual study data were included; we used them to estimate outcome measures using a random-effects model. All primary and subgroup analyses were performed using Excel and R software; a P value of 0.05 was considered statistically significant.

RESULTS

In this systematic review and meta-analysis, we included a total of 1319 patients, of which GTR, N = 269 (20.3%), and STR, N = 14 (1%), were total. Table 1-3, while in Table 1-Figure 2, we included N = 931

(70.5%) patients, GTR, N = 207 (15.6%), and one STR, N = 9 (0.6%). Therefore, in table 2, figure 3.321, 24.3% of patients had pontine cavernomas (N=210), 16% had midbrain cavernomas (N=83), and 6.2% had medulla oblongata cavernomas (N=48). Table 3, figure 4, GTR, N=62 (4.7%) and STR, N=5 (0.37%) patients. A study conducted in mid-2020 prospectively based, according to the database, on 802 patients who were treated with microsurgical surgery for cavernous malformations, of which 213 patients were brainstem, through a retrospective search according to recurrence and primary resection for a second reintervention.

The BCM, due to its proximity to the tractors and cranial nerve nuclei, makes it difficult to penetrate or enter normal tissue to access the lesion from the tissue that is adjacent and normal according to the plane that separates it. There is an interaction according to tissue sensitivity and the elective extreme, occasionally making it difficult to avoid or leave remnants of tissue, because recurrences increase morbidity and surgical reinterventions. 6.6% of patients underwent reintervention, while 34 series of hemorrhages were observed, whose recurrence rate in these was 5.9% per year; the median hemorrhage covered 897 days. The frequency ranged from the pons and the midbrain to the medulla oblongata.

A blind spot in the surgical corridor was found to be the most frequent cause of BCM. Detecting recurrence in the first 6 months is difficult, as the resection bed has healed. Knowledge of the right-angle method is essential, as it helps anticipate these blind spots after intensively searching the resected cavity to detect residual BCM at the time of surgery. This reduces recurrence to a minimum. Garcia R et al. [6, 54, 55].

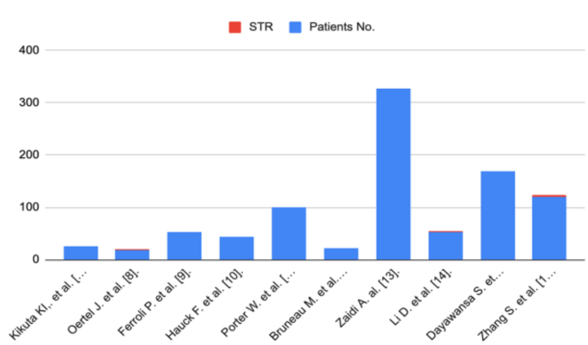

Figure 2. Graphic representation of comparative studies of cavernous malformations affecting the brainstem, showing gross total resection (GTR) versus subtotal resection (STR).

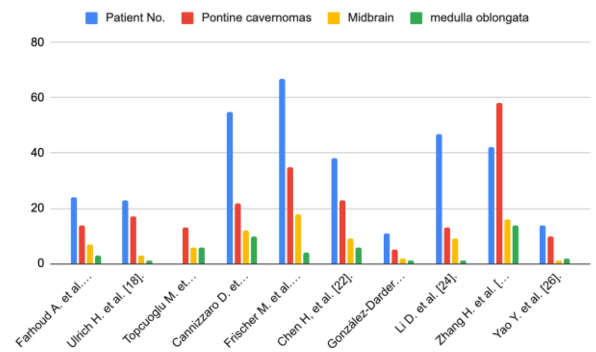

Figure 3. Graphs of patients with cavernous malformations affecting the brainstem, pons, midbrain, and medulla (BCM).

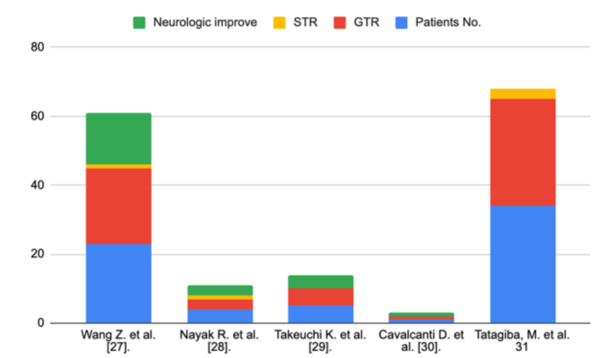

Figure 4. Graphic representation of patients, showing surgical resection and postoperative results of neurological recovery after surgery.

Additionally, Hu et al. An optimal surgical approach is sought to obtain the best results according to the anatomical location of the brainstem malformation lesions. A review of 15 articles based on the endonasal endoscopic approach and the transcranial endoscopic approach for BCM resection in 19 patients was conducted. These approaches are most frequently used due to their easy illumination of the surgical field depth with excellent vision. Ventral axial BCMs are also added to the endonasal endoscopic approaches in two directions. It is also worth noting that endoscopic use is of great importance for cavernous hemangiomas on the dorsal aspect of the brainstem because it provides the best field of view, minimizing the need for brain retraction during surgery. The overall endoscopic resection rate was 81%. Five patients underwent CSF leak repair for lesions measuring 2 cm in diameter. Of these five patients, three had rhinorrhea as a postoperative complication. Most patients showed significant improvement, demonstrating the effectiveness of this approach in an experienced surgeon. [32, 56, 57].

Brainstem cavernoma malformations (BCMs) tend to develop sequential hemorrhages and chronic neurological deficits. [33]. Rebleeding may occur in up to 45% of cases per year; therefore, this pathology reaches the pial ependymal surface, requiring surgical management and associated morbidity. [34, 35, 58]. There are reports linking venous developmental anomalies (DVAs) and cavernous malformations of the brainstem in 13% to 40% of cases. [36, 37, 59]. DVAs are considered specific variants of the medullary veins, which in turn represent the compensated venous drainage system, all due to aplasia or hypoplasia, which rapidly occludes normally developing veins. [38, 39, 60]. Additionally, magnetic resonance imaging combined with angiography is replacing angiography in almost all cases of DVAs and BCM as a noninvasive variant. [40, 41, 61].

Approach and resection of cavernous malformation

Once the exophilic structural field of the cavernous malformation has been visualized inferior to the fifth cranial nerve, we create a dissection plane with fine bayonet forceps. The cavernoma will be slowly resected with the developed hematoma. We begin to excise the lower portion of the cavernoma using gentle manual traction with the dominant hand and, once dissected, suction with the non-dominant hand. This method allows us to extract or dissect the lower pole of the cavernoma, which extends to the medulla oblongata. After resecting the lower part of the brainstem, we continue with the superior pons and focus on the fifth cranial nerve. Since the hemosiderin-containing tissue is present above and below the fifth cranial nerve, it will connect with the upper pole of the cavernoma.

Once the cavernoma is observed, we proceed with a corticectomy superior and superior to the fifth cranial nerve. Using fine bayonet forceps, we created a plane between the cavernoma and the surrounding gliotic tissue itself or around it. We will proceed to widen both corridors through corticectomy, which will facilitate safer resection of the cavernoma. Once again, gradual excision is performed through gentle suction dissection. If the patient has had prior surgeries, there is a possibility of adhesion of the lesion, which will require a sharper resection with microscissors to free the cavernoma. Finally, once the deep venous anomaly, which runs in the middle of the protuberance, has been identified. Perhaps because there was a residual cavernoma adherent to the developmental venous anomaly (DVA), it will be dissected with microscissors, because preserving the DVA is essential to prevent venous infarction. [42].

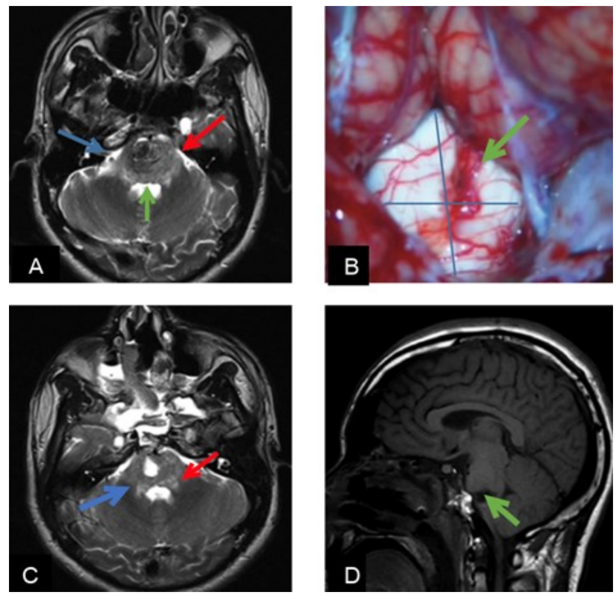

Figure 5. a) Preoperative axial image; b) Approach to the cavernoma (see blue and green arrows). c) Postoperative axial T2-weighted MRI (see red and blue arrows). d) Postoperative sagittal T1-weighted MRI (see green arrow).

Retrosigmoid approach for brainstem cavernous malformation

The patient is placed in the 3/4 prone position with the head rotated toward the side ipsilateral to the lesion and flexed. A sigmoid incision is made approximately 3 cm posterior to the superior border of the auricle, extending through the asterion to the midnuchal line. A retrosigmoid craniotomy is then performed, followed by a posterior partial mastoidectomy to expose the inferior border of the transverse sinus and the posterior border of the sigmoid sinus. We continue draining 50 ml of CSF from the lumbar drain before opening the dura to allow brain relaxation. We open the dura mater in a crosswise fashion, as well as the arachnoid membrane of the cisterna magna, and release more CSF using the Dandy maneuver. We retract the lateral aspect of the cerebellar hemisphere medially and expose the facial and vestibulocochlear nerves.

We continue medially to the junction of the tentorium with an insertion of the petrous bone until we find the trigeminal nerve. We continue coagulating and sectioning the superior petrosal vein, and after opening the arachnoid membranes of the ambient and quadrigeminal cisterns to allow for greater CSF outflow, once the injury is dissected and corrected, we proceed to close the approach. [43].

Discussion

Brainstem cavernoma malformation: there are multiple recommended surgical approaches, including the orbitozygomatic pterional approach, the supracerebellar infratentorial approach, the retrosigmoid approach, midline suboccipital craniotomy, and far lateral suboccipital with or without telovelar resection. [44]. Noting that the central paramedian portion and the deep portion of the medulla oblongata are difficult to access surgically. The BCM, central pontomedullary and paramedian, are approached through a retrosigmoid approach and a middle cerebellar transpenducular approach. [45, 46]. Continuing the dissection through the middle cerebellar peduncle approximately 1 cm to the central or paramedian pons, we will approach it with caution due to the risk of involvement of the central pontomedullary cavernoma and the developmental venous anomaly with the brainstem, which drains from the middle cerebellar peduncle vein, which will lead to a high risk of venous infarction. of the brainstem or an approach through the pontomedullary sulcus. [47].

Anatomy of the Brainstem

Its rostral portion is the midbrain, which is represented by four pons: the pons extending from the superior and inferior colliculi to its dorsal or posterior surface, and the superior cerebellar pedicles, which contain the descending corticospinal or corticopontine tracts, on its ventral or anterior surface; the nuclei of the third and fourth cranial nerves, and the sensory part of the fifth, as they meet in the midbrain. The ascending superior cerebellar peduncles, upon crossing, decussate toward the caudal midbrain. The fibers enter the red nucleus and continue to the thalamus. The midbrain also consists of the substantia nigra and the ventral tegmental area, both containing dopamine, the pedunculopontine nucleus, and the first raphe nucleus. Caudal to the midbrain, we find the pons. [48]. From here, the corticopontine fibers terminate in the so-called pontine nuclei; the axons give rise to the cerebellopontine fibers, which cross in the midline to form the middle cerebellar peduncle, which is a vulnerable site for injury in malnourished individuals, probably due to rapid electrolyte correction.

This is especially true due to myelin disruption, resulting in what is known as central pontine myelinolysis; osmotically active factors are expelled from cells within the gray matter, which are toxic to myelin. [49]. We will find the white matter adjacent to an edematous gray matter; the pontocerebellar fibers will be crossed, as if intermingled with each other, with the pontine nuclei and will be more exposed. The tracts of ascending and descending fibers will also be compacted with the white matter bundles and will be less affected by them. There will be other lesions, for example, in the gray matter with densely myelinated fibers, in the thalamus, as in the basal ganglia and the cerebellum itself.

Then, caudal to the pons, we find the medulla oblongata, containing the nuclei of cranial nerves IX, X, XI, and XII and part of cranial nerve V. Next, we find the ascending spinocerebellar tracts that form the inferior cerebellar peduncle. The ascending sensory tracts will emerge from the body or posterior columns, terminating in the nuclei of the posterior column of the gracilis and cuneate nuclei at the lower level of the medulla oblongata. These nuclei originate from the spinothalamic tracts, which intersect with a sensory decussation. Below the medulla oblongata, they ascend to form the medial lemniscus. [50].

Monitoring of the brainstem

Brainstem injuries are more common than in other areas of the central nervous system, as surgical morbidity will depend on the high concentration of neuronal structures that are certainly altered or distorted, as they are unrecognizable under a microscope. Using intraoperative neurophysiological mapping will alert us to neuronal structures in critical condition, allowing us to avoid injuring them. By performing a transfloor approach to the fourth ventricle, we will identify the facial colic and, at the same time, the triangles of the vagus and hypoglossal nerves, which will allow us to enter and access the brainstem through safe areas, the suprafacial and intrafacial triangles, with minimal injury. [60]. Corticospinal tract mapping will be performed in cases of brainstem resection adjacent to the corticospinal tract. Neurophysiological monitoring techniques will also include corticobulbar motor evoked potentials and brainstem auditory evoked potentials with somatosensory evoked potentials. It will simultaneously provide comprehensive feedback on the functionality of the neural pathways and allow the surgeon time to appropriately reconsider and correct the surgical injury through an excellent monitoring strategy.[51, 61, 62].

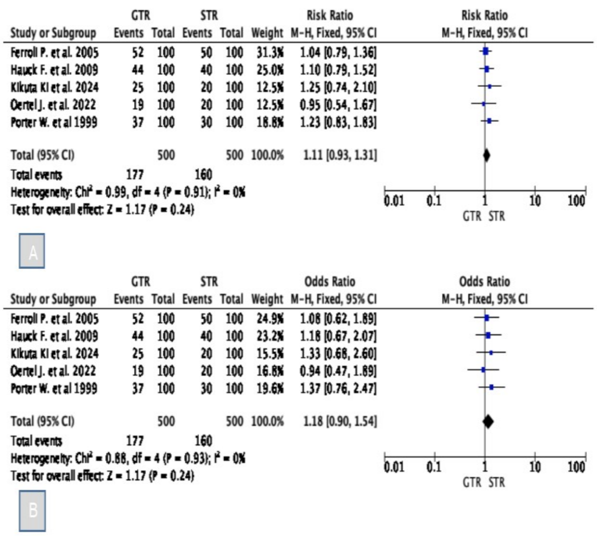

Figure 6. a,b) Forest plot of studies related to the management of brainstem cavernous malformations (BCM), Risk-ratios vs odd ratio.

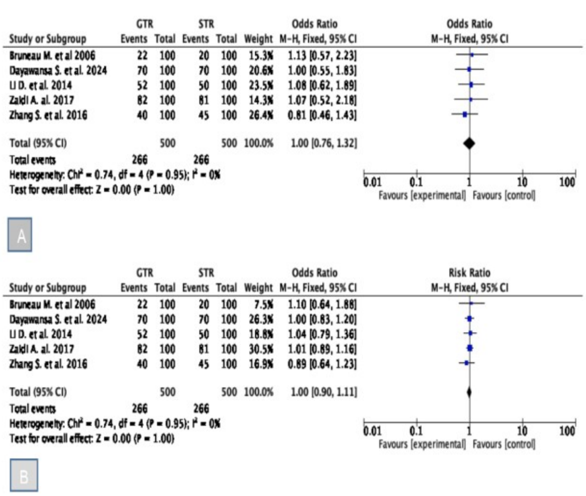

Figure 7. a,b) Forest plot of studies related to the management of brainstem cavernous malformations (BCM), odd ratios vs risk ratio; gross total resection and subtotal resection.

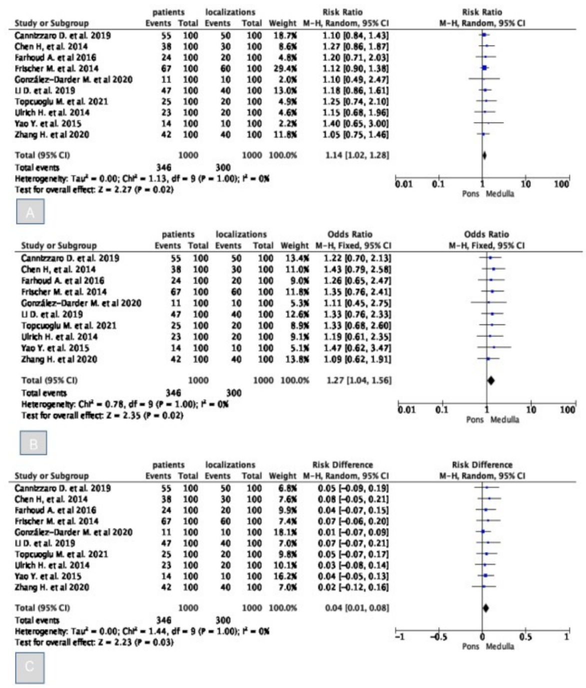

Figure 8. a, b, c) Forest plot of studies related to the management of brainstem cavernous malformations (BCM), risk ratio vs. odds ratio and risk difference; in terms of location: brainstem, pons, medulla.

Limitations And Future Directions

In this review, we emphasize the limitations present in studies related to endonasal endoscopy for cavernous malformations of the brainstem, such as the presence of rebleeding or hemorrhage, which required reintervention, evacuation, or drainage. It should be emphasized that intraoperative injuries that generated fistulas or cerebrospinal fluid (CSF) leaks, as well as rhinorrhea, may or may not be possible. Microsurgical resection is very complex, so a total gross resection is impossible in many cases, resulting in a subtotal resection, which will require stereotaxy and radiosurgery. Many authors debate whether or not to operate on the brainstem, as previous studies showed high rates of postsurgical lesions, including quadriplegia, so endoscopic removal is the preference of many specialists. Regarding the future of BCM resection, we will continue with 3D prints from the patient's scanner to better understand the approach, as well as neuronavigation and neuromonitoring to achieve optimal postoperative results and reduce neurological complications, thus improving the patient's recovery and rehabilitation status. [52]. [53, 63].

Conclusion

This study shows that microsurgical resection of cavernous malformations of the brainstem is not only a complex issue in terms of the treatment of this pathology, but we also compared previous approaches from 10 to 15 years ago, and the difference in postsurgical complications was greater. Even so, endonasal endoscopy is gaining more and more strength, since 80% of resections, even with complications, have been very effective in terms of rehabilitation and postoperative follow-up, but even so, the recurrences are impossible to reach. Stereotactic radiosurgery is still recommended, and symptoms such as dysphagia or phonation will be recovered through conservative treatment of the patient. Also, the management of cerebrospinal fluid leaks will require a postoperative reintervention to correct the problem in question.

Table 1. Comparative studies of cavernous malformations affecting the brainstem, with the types of approaches and surgical procedures to be demonstrated.

Author	Year	Kind of Study	Patients No.	Age range	Pathology	Approch	GTR/	STR	hemorrhages	Follow up
Kikuta KI,. et al. [7].	2024	retorspective	25	13 to 61 years (mean ± SD = 37 ± 12 years	Brainstem cavernous malformation	CMB mricrosurgery	24	1	7 ± 1.0	1 year
Oertel J. et al. [8].	2022	retrospective	19	53.5 (± 11.1) years	Cavernous malformation	The binostril transsphenoidal transclival / 16 microscope	18	1	+	27.8 (12-89) months
Ferroli P. et al. [9].	2005	Retrospective	52	N/A	BCM	anterolateral pontine	+	-	3.8%	1.5–10.5 yr
Hauck F. et al. [10].	2009	Retrospective	44	N/A	BCM	Surgical resection	+		N/A	11 months
Porter W. et al. [11].	1999	retrospective	100	37	BCM	PONS	+	-	5%	N/A
Bruneau M. et al. [12].	2006	retrospective	22	N/A	(BSCs	Surgical resection	+	-	N/A	44.9 months
Zaidi A. al. [13].	2017	retrospective	327	≥18 years	BSCMs	Surgical resection	+	-	N/A	6 weeks
Li D. et al. [14].	2014	Retrospective	52	1-17 years	CMs	Surgical	49	3	12.3% and 32.5%	7.9 years
Dayawansa S. et al. [15].	2024	retrospective	170	37.3	CCM)	stereotactic radiosurgery (SRS)	+		77.6%	3.4 years
Zhang S. et al. [16].	2016	Retrospective	120	40.29 ± 14.78 years	BCM	microsurgery	116	4	4.2% and 42.9%,	50.7 ± 26.5 months

Table 2. Shows the most frequent locations of cavernous malformations that alter the brainstem (BCM).

Author	research	Year	Patient No.	Pontine cavernomas	Midbrain	medulla oblongata	Approach	Follow up
Farhoud A. et al. [17].	Retrospective	2016	24	14	7	3	midline suboccipital	1
Ulrich H. et al. [18].	Retrospective	2014	23	17	3	1	Suboccipital/retrosigmoidea	N/A
Topcuoglu M. et al. [19].	Retrospective	2021	25	13	6	6	25	N/A
Cannizzaro D. et al. 20	Retospective	2019	55	22	12	10	Lateral terosigmoideo/far lateral,	63.4 months
Frischer M. et al. [21].	retrospective	2014	67	35	18	4	Suboccipital medial /lateral	2 years
Chen H, et al. [22].	Retrospective	2014	38	23	9	6	Suboccpital middle, subtemporal trantentorial	N/A
González-Darder M. et al. [23].	Prospective	2020	11	5	2	1	Peritrigeminal rostrally to the cochleo-vestibular-facial bundle	1 year
Li D. et al. [24].	RCT	2019	47	13	9	1	preoperative diffusion tensor imaging (DTI) and diffusion tensor tractography (DTT)	35.7 years
Zhang H. et al. [25].	Retrospective	2020	42	58	16	14	diffusion tensor tractography (DTT)	N/A
Yao Y. et al. [26].	Retrospective /case series	2015	14	10	1	2	White matter tractography of corticospinal tracts (CSTs	N/A

Author	Research	year	Patients No.	GTR	STR	Neurologic improve	Follow up
Wang Z. et al. [27].	Case series	2015	23	22	1	15	3.5 years
Nayak R. et al. [28].	Case series	2015	4	3	1	3	2 years
Takeuchi K. et al. [29].	Case series	2023	5	5	0	4	N/A
Cavalcanti D. et al. [30].	Case report	2020	1	1	N/A	1	3 Months
Tatagiba, M. et al. 31	Case series	2023	34	31	3	N/A	N/A

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