

PREOPERATIVE ONYX EMBOLIZATION OF INTRACRANIAL ARTERIOVENOUS MALFORMATIONS: A SINGLE CENTER EARLY EXPERIENCE

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Introduction. Intracranial arteriovenous malformations (AVM) are considered one of the life-threatening pathologies which are challenging to manage. Endovascular embolization of intracranial AVMs is a line of management which developed over the past two decades to downgrade the lesion, a step is thought to make surgeries of more favorable outcome.

Patients and methods. All patients who were diagnosed with brain AVM in Mansoura University Hospitals between January 2017 through December 2022 were retrospectively analyzed. Clinical and radiological outcome were studied, as well as surgeons' satisfaction and procedural difficulties.

Results. Nine patients met the criteria for multimodal management, seven of them were female, mean age of the group 36 years. Patients' mRS remained unchanged after embolization sessions, one patient had an added neurological deficit in the form of increased severity of motor deficit after surgery, which was reversible during follow up period, mean follow up period is 103 days.

Conclusion. Pre-operative embolization is a safe tool to be added to the multi-modal treatment of high grades cerebral AVM's with good outcome and feasible surgical technique.

Keywords: intracranial arteriovenous malformations, multi-modal treatment, hybrid techniques, Onyx embolization, preoperative embolization

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Предоперационная эмболизация с использованием системы Онух при внутричерепных артериовенозных мальформациях: ранний одноцентровой опыт

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Введение. Внутричерепные артериовенозные мальформации (АВМ) – угрожающие жизни, сложные для лечения патологии. Эндоваскулярная эмболизация внутричерепных АВМ была разработана в последние 2 десятилетия для снижения степени тяжести мальформации, что предположительно приводит к более благоприятным исходам хирургического лечения.

Пациенты и методы. Проведен ретроспективный анализ данных всех пациентов, которым был поставлен диагноз АВМ головного мозга в больницах университета Мансура в период с января 2017 г. по декабрь 2022 г. Изучены клинические и радиологические исходы, а также степень удовлетворенности хирурга и сложности в ходе процедуры.

Результаты. Девять пациентов соответствовали критериям мультимодального лечения, в том числе 7 женщин. Средний возраст пациентов составил 36 лет. У всех пациентов сумма баллов по модифицированной шкале Рэнкина после эмболизации не изменилась. У 1 пациента после операции развился дополнительный неврологический дефицит в форме усиления двигательного дефицита, который вернулся на исходный уровень в период наблюдения. Средняя продолжительность наблюдения составила 103 дня.

Заключение. Предоперационная эмболизация – безопасный метод, характеризующийся благоприятными исходами и выполнимой хирургической методикой, который следует использовать как часть мультимодального лечения тяжелых АВМ головного мозга.

Ключевые слова: внутрисерпные артериовенозные мальформации, мультимодальное лечение, гибридные методы, эмболизация Опух, предоперационная эмболизация

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INTRODUCTION

Intracranial arteriovenous malformations are considered among the most life-threatening pathologies which are challenging to manage. So far, the minority of these cases have been subjective to firm applicable algorithm of management. On the other hand, higher grades of this pathology are yet subjective to personal and institutional experience with wide range of treatment options which represent a rich material for applied scientific research.

The widely used Spetzler–Martin grading system is based mainly on size of lesion, location and venous drainage. This grading system has proven quality to choose the best treatment option. Accordingly, grades I and II are surgical, while grades III through V are subjective to multimodal treatment [1].

Grade III and higher lesions are challenging to resect as they are heterogenous group of lesions with different sizes, locations and venous drainage patterns. These criteria make it difficult to form a solid algorithm for management [2].

Endovascular embolization of intracranial arteriovenous malformations is a line of management which developed over the past two decades, it can be employed solely as a single treatment option, or as a step that facilitates surgical resection [3].

Recent case series has proven a favorable outcome of surgery following pre-operative embolization. In this study, we retrospectively analyze the cases who underwent preoperative embolization for intracranial arteriovenous malformation surgery.

PATIENTS AND METHODS

All patients who were diagnosed with brain arteriovenous malformations (AVM) in Mansoura University Hospitals between January 2017 through December 2022 were retrospectively analyzed. Institutional Review Board agreement was obtained from Mansoura University IRB committee, a waiver for patient consent was granted due to the retrospective nature of the study. Microsurgical resection was performed by one of two neurosurgeons (A.E. and M.K.), while the whole team participated in preoperative embolization.

A survey tool (Fig. 1) was created to measure the overall satisfaction of the operating surgeons based on their cumulative experience with cases in comparison to their usual practice without preoperative embolization.

Patients' charts were retrospectively reviewed for clinical data and radiological data, including presentation, complications, treatments, neurological outcomes, modified

	Non-embolized			Embolized	
Field visibility	1	2	3	4	5
Shorter direction of dissection	1	2	3	4	5
Identification of feeder	1	2	3	4	5
Feeders control	1	2	3	4	5
Cutting of feeder	1	2	3	4	5
Identification of drainage	1	2	3	4	5
Dissection of nidus	1	2	3	4	5
Nidus excision	1	2	3	4	5

Fig. 1. Survey tool for surgeons to evaluate feasibility of the surgical procedure, where 1 score is totally favoring non-embolized cases, while 5 score favors preoperative embolization, hence score of 3 is equivocal

Rankin scale (mRS) scores and imaging studies, as well as operative data such as blood loss and intraoperative complications.

Spetzler–Martin grading system was adopted to classify lesions included in the study. Patients who presented with AVM susceptible for pre-operative embolization were only included i. e. grade III and higher. Patients with grades I and II were excluded as surgery alone is the line of management. Patients whose management included more than those two lines, e. g., gamma knife and multiple surgeries, were excluded.

RESULTS

During 18 months, 9 patients met the criteria for multimodal management, 7 of them were female, mean age of the group 36 years. At presentation, 8 patients were neurologically intact while two showed neurological deficits in the form of motor weakness and aphasia. Six lesions' Grade was III, while three lesions were of grade IV. Criteria of the lesions are summarized in Tables 1 and 2.

Patients' mRS remained unchanged after embolization sessions, 1 patient had an added neurological deficit in the form of increased severity of motor deficit after surgery, which was reversible during follow up period, mean follow up period is 103 days.

Patients needed multiple sessions were 2, mean time interval between last embolization session and surgery was 10 days (range 6 to 14).

The survey was completed by the two senior surgeons who participated in all cases either as main surgeon or as supervising professor. One surgeon, (A.E.), reported mild favorability (4/5) in all aspects of surgery, except for cutting the feeder arteries where this step was slightly favorable (2/5) for the non-embolized cases surgery, with mean score

of (3.7/5). On the other hand, the other surgeon reported higher favorability for previously embolized cases in all aspects; complete favorability (5/5) for field visualization, shorter duration of dissection, dissection of nidus and nidus excision, while mild favorability (4/5) for other aspects i. e. identification of feeder, feeder control and cutting.

Table 1. Location of lesions

Location	No. of cases
Frontal	3
Temporal	3
Parietal	2
Occipital	1
Cerebellar	1

Table 2. Spitzler–Martin Grading of lesions

Parameter	No. of cases
Size:	
<3 cm	0
3–6 cm	8
>6 cm	1
Eloquence	6
Deep venous drainage	2

ILLUSTRATIVE CASE

Female patient, 27 years old, presented with intractable seizures, on examination patient showed non-remarkable neurological examination. Magnetic resonance imaging of the brain showed left (dominant) temporal AVM. The lesion was of Spetzler–Martin grade III (size 2/eloquence 1/venous drainage 0).

Patient underwent preoperative embolization, followed by surgical excision. Surgery was uneventful with blood loss around 450 ml, patient postoperative status as preoperative with improved seizures control on single anti-epileptic during follow up (Fig. 2).

DISCUSSION

Arteriovenous malformations of the brain are considered among the most challenging central nervous system lesions to treat, such pathologies carry a lifetime risk of hemorrhage and subsequent mortality and morbidity which makes intervention mandatory in most cases [4]. Given their unique individual disruption of the normal cerebral vasculature, each case should be assessed and studied solely to conclude an efficient treatment plan.

Due to their chaotic nature and uneven patterns, several classification systems have been proposed, despite that, Spetzler–Martin [1] classification which was published in 1986 remains the worldwide identity of each AVM case. According to this grading system, low grades lesions (I, II)

are predicted to have good favorable outcome after microsurgical resection due to their simple anatomy, while grade III and higher grades are difficult to manage as they straddle the limit of operability for many neurosurgeons [5, 6], such lesions are composed of heterogenous group with various sizes, deep venous drainage and/or eloquent location which makes no clear algorism of treatment applicable so far.

Any treatment plan for AVM lesion should include one or more line of management: observation, microsurgery, endovascular embolization and radiosurgery. Microvascular resection provides optimal obliteration rate and favorable outcome [7, 8]. However, it carries higher risks of neurological deficits for high grade lesions which is reported to be 31 % and 37 % for grades IV and V respectively [9]. Therefore, high grades AVM's require multimodal management plan.

Multimodal paradigm expected results for high grade AVM's vary according to the lines of management involved, endovascular embolization followed by stereotactic radiosurgery results in a low obliteration rate of approximately 42–44 % [10] in comparison to approximately 98 % obliteration rate for SRS followed by surgery [11]. On the other hand, binary management using preoperative embolization followed by microsurgical resection is most widely treatment option recently.

The hypothesis for preoperative embolization is mainly based on decreasing the blood flow and volume through the nidus which decreases bleeding during surgery as well as facilitates microsurgical resection in a less bloody and more visible field [5]. Previous reports concluded that preoperative embolization had no positive effect on intraoperative blood loss despite better outcome [12], this can be attributed to uncalculated blood loss during microsurgical procedures [13]. However, this study didn't compare embolization to non-embolization group, mean blood loss volume for the group was below average that reported in literature.

The shortcoming of preoperative embolization technique is exposing patients to complications of both procedures; endovascular management such as catheter stinking, intraoperative hemorrhage, and embolization-induced normal perfusion pressure breakthrough as well as surgical risk. In addition, any staged procedure exposes the patient to the risk of hemorrhage, ischemia and/or edema during the interval between procedures due to the unpredicted course of the disease following partial embolization [3]. Therefore, the ideal interval between embolization and surgery remains unclear and not fully investigated. However, it's believed that once session technique i. e., hybrid surgery, is a promising innovation to reduced risk and complications.

The choice of preoperative embolic material might be debatable to some practitioners, as per multicentric randomized control trial and a few observational studies, there is no superiority of one embolic agent over the other

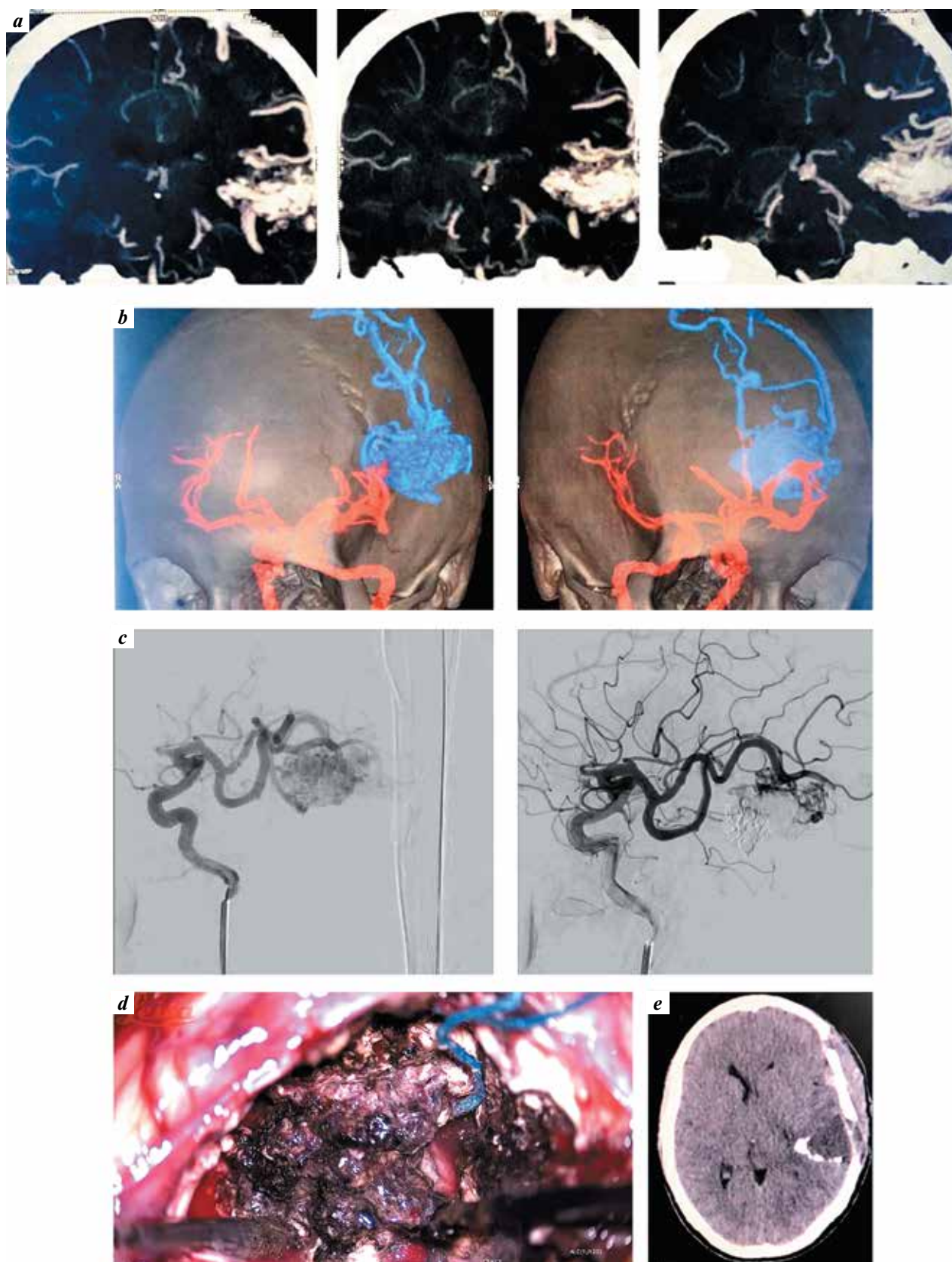


Fig. 2. Patient examination data: a — computed tomography angiography of the cerebral arteries, showing left posterior temporal arteriovenous malformation, with 5 cm nidus; b — 3D reconstruction of cerebral angiography showing superficial venous drainage of the nidus; c — digital subtraction angiography showing pre and post embolization, with residual nidus as part of pre-operative embolization; d — intraoperative microscopic image showing embolized arteries with Onyx; e — postoperative computed tomography scan showing the cavity of excised lesion, postoperative oedema and remnants of the Onyx cast at the bed of the lesion

regarding preoperative embolization [14, 15]. However, the advantages of Onyx embolizing agent over N-butyl cyanoacrylate (NBCA) for brain AVM embolization generally is clear. Formerly, NBCA was adopted as the only available embolic agent with success rate which reached 90 % obliteration rate in some studies despite technical difficulties. Using NBCA requires multiple sessions of embolization with limited maneuverability and inability to penetrate small vessels due to its adhesive nature, as well as flow dependent behavior [16]. On the other hand, since introduction of Onyx to this field, it showed greater superiority due to its cohesive nature, ability to diffuse through small vessels and diffusion in a flow independent pattern which allows plug and push technique to form a cast reaching deeper in the nidus through either arterial axis or venous axis. Therefore, Onyx achieves deeper penetration into the nidus which is of a great value as it results in downgrading the lesion via decreasing the size of the nidus and/or obliteration of deep venous drainage if achieved [17–19].

According to T. Izumo et al. [20], histopathological examination of surgically excised AVM's following preoperative embolization showed remaining erythrocytes inside the nidus despite angiographic resolution for cases who underwent preoperative embolization using NBCA, in comparison to complete Onyx cast with no erythrocytes for the Onyx group concluding that NBCA embolization is considered more of a feeder occlusion procedure than nidus occlusion.

Although feeder occlusion is considered an unsatisfactory procedure in cases where only endovascular embolization is adopted as a stand-alone treatment option [21], it is one

of the goals of preoperative embolization to decrease flow inside the nidus and to avoid premature closure of draining veins which is one of the most catastrophic intraoperative complications. This may explain the previously mentioned results of non-superiority of Onyx over NBCA regarding preoperative embolization procedures, as NBCA embolization achieves this goal.

Technical difficulty to excise a previously embolized AVM is reported by several neurosurgeons as the hard Onyx cast occupying the nidus makes it hard and non-compressible also the edges of the cast are sharp to surrounding brain tissue during excision [22], previously embolized arterial feeder is extremely difficult to cut using micro scissors which requires introduction of larger instruments to a microscopic field. According to our survey, the step of cutting previously embolized feeders was less favorable for one surgeon (2/5) but slightly favorable by the other (4/5). However, there was overall satisfaction by the two surgeons, this concept when added to measurable outcomes, especially blood loss, makes preoperative embolization a promising step to be added to the armaments against such lesions.

CONCLUSION

Pre-operative embolization is a safe tool to be added to the multi-modal treatment of high grades cerebral AVM's with good outcome and feasible surgical technique, it's value to reduce blood loss and surgery time, feeder occlusion is an achievable goal before surgery. Further studies should be adopted to evaluate surgeon's favorability of the procedure via strictly measurable outcomes.

REFERENCES / ЛИТЕРАТУРА

- Spetzler R.F., Martin N.A. A proposed grading system for arteriovenous malformations. *J Neurosurg* 1986;65(4):476–83. DOI: 10.3171/jns.1986.65.4.0476
- Catapano J.S., Frisoli F.A., Nguyen C.L. et al. Spetzler–Martin grade III arteriovenous malformations: a multicenter propensity-adjusted analysis of the effects of preoperative embolization. *Neurosurgery* 2021;88(5):996–1002. DOI: 10.1093/neuros/nyaa551
- Del Maestro M., Luzzi S., Gallieni M. et al. Surgical treatment of arteriovenous malformations: role of preoperative staged embolization. *Acta Neurochir Suppl* 2018;129:109–13. DOI: 10.1007/978-3-319-73739-3_16
- Van Beijnum J., van der Worp H.B., Buis D.R. et al. Treatment of brain arteriovenous malformations: a systematic review and meta-analysis. *JAMA* 2011;306(18):2011–9. DOI: 10.1001/jama.2011.1632
- Lawton M.T.; UCSF Brain Arteriovenous Malformation Study Project. Spetzler–Martin Grade III arteriovenous malformations: surgical results and a modification of the grading scale. *Neurosurgery* 2003;52(4):740–8; discussion 748–9. DOI: 10.1227/01.neu.0000053220.02268.9c
- Fleetwood I.G., Marcellus M.L., Levy R.P. Deep arteriovenous malformations of the basal ganglia and thalamus: natural history. *J Neurosurg* 2003;98(4):747–50. DOI: 10.3171/jns.2003.98.4.0747
- Derdeyn C.P., Zipfel G.J., Albuquerque F.C. et al. Management of brain arteriovenous malformations: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2017;48(8):e200–e24. DOI: 10.1161/STR.0000000000000134
- Choi J.H., Mohr J.P. Brain arteriovenous malformations in adults. *Lancet Neurol* 2005;4(5):299–308. DOI: 10.1016/S1474-4422(05)70073-9.
- Spetzler R.F., Ponce F.A. A 3-tier classification of cerebral arteriovenous malformations. *J Neurosurg* 2011;114(3):842–9. DOI: 10.3171/2010.8.JNS10663
- Patibandla M.R., Ding D., Xu Z., Sheehan J.P. Stereotactic radiosurgery for pediatric high-grade brain arteriovenous malformations: our experience and review of literature. *World Neurosurg* 2017;102:613–22. DOI: 10.1016/j.wneu.2017.03.064
- Abla A.A., Rutledge W.C., Seymour Z.A. et al. A treatment paradigm for high-grade brain arteriovenous malformations: volume-staged radiosurgical downgrading followed by microsurgical

- resection. *J Neurosurg* 2015;122(2):419–32.
DOI: 10.3171/2014.10.JNS1424
12. Donzelli G.F., Nelson J., McCoy D. et al. The effect of preoperative embolization and flow dynamics on resection of brain arteriovenous malformations. *J Neurosurg* 2020;132(6):1836–44. DOI: 10.3171/2019.2.JNS182743
13. Kollberg S.E., Häggström A.C.E., Lingehall H.C., Olofsson B. Accuracy of visually estimated blood loss in surgical sponges by members of the surgical team. *AANA Journal*. 2019;87(4):277–84.
14. Loh Y., Duckwiler G.R.; Onyx Trial Investigators. A prospective, multicenter, randomized trial of the Onyx liquid embolic system and N-butyl cyanoacrylate embolization of cerebral arteriovenous malformations: Clinical article. *J Neurosurg* 2010;113(4):733–41. DOI: 10.3171/2010.3.JNS09370
15. Crowley R.W., Ducruet A.F., Kalani M.Y.S. et al. Neurological morbidity and mortality associated with the endovascular treatment of cerebral arteriovenous malformations before and during the Onyx era. *J Neurosurg* 2015;122(6):1492–7. DOI: 10.3171/2015.2.JNS131368.
16. Raupp E.F., Fernandes J. Does treatment with N-butyl cyanoacrylate embolization protect against hemorrhage in cerebral arteriovenous malformations? *Arq Neuropsiquiatr* 2005;63(1):34–9. DOI: 10.1590/s0004-282x2005000100007
17. Natarajan S.K., Ghodke B., Britz G.W. et al. Multimodality treatment of brain arteriovenous malformations with microsurgery after embolization with Onyx: single-center experience and technical nuances. *Neurosurgery* 2008;62(6):1213–25; discussion 1225–6. DOI: 10.1227/01.neu.0000333293.74986.e5
18. Weber W., Kis B., Siekmann R. et al. Preoperative embolization of intracranial arteriovenous malformations with Onyx. *Neurosurgery* 2007;61(2):244–52; discussion 252–4. DOI: 10.1227/01.NEU.0000255473.60505.84
19. Gross B.A., Jankowitz B.T., Friedlander R.M. Cerebral intraparenchymal hemorrhage: a review. *JAMA* 2019;321(13):1295–303. DOI: 10.1001/jama.2019.2413
20. Izumo T., Okamura K., Takahira R. et al. Impact of pre-operative embolization with Onyx for brain arteriovenous malformation surgery. *Front Neurol* 2022;13:875260. DOI: 10.3389/fneur.2022.875260
21. Van Rooij W.J., Sluzewski M., Beute G.N. Brain AVM embolization with onyx. *AJNR Am J Neuroradiol* 2007;28(1):172–7; discussion 178.
22. Baskaya M. Preoperative AVM embolization: useful or not? Miami: Miami University Neurosurgery Webinar 23.7.2020.

Authors' contributions

M.M. Elsherbini, M.M. Nabeeh, M.A. Kassem, A. Ezz Eldin, M. Farouk: conception and design, provision of study material or patient's data, collection and assembly of data, data analysis and interpretation, article writing.

Вклад авторов

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