The Preoperative Functional Downgrading of Brain AVMs

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Introduction

Treatment options for brain arteriovenous malformations (AVMs) include microsurgical resection, transarterial or transvenous catheter-based embolization, radiosurgery, or a combination of these. From the surgical standpoint, Spetzler-Martin (SM) grade III AVMs pose more special challenges than doing grades I and II because of their frequent deep-seated location, common vascular supply from the lenticulostriate, or thalamostriate arteries, and a not unusual racemose nidal angioarchitecture. On the other hand, deeper arterial feeders have been reported to be pivotal in determining the morbidity and resectability of middle-sized AVMs [1–4]. In principle, the preoperative embolization of the deeper arterial feeders, as well as the increasing of the compactness of the nidus, may both lead to an easier dissection, helping the hemostasis and ultimately reducing intraoperative blood loss. Although the literature reports many studies about the utility of the preoperative embolization of brain AVMs, too few of them stay focused on the technical details to be implemented to maximize the effectiveness and safety of the treatment.

Throughout a retrospective review of an institutional series, the present study is aimed to report the key technical aspects of the preoperative endovascular-based functional downgrading of SM grade III brain AVMs, as well as those factors underlying its effectiveness and safety.

Material and Methods

Data of 97 patients consecutively treated for a brain AVM were retrospectively reviewed. Only SM grade III malformations that underwent a combined endovascular-surgical treatment were selected, resulting in 31 overall treated cases. Table 1 summarizes patients' demographics, the prevalence according to the location, and the clinical onset of the analyzed surgical series (Table 1). By default, preoperative imaging included CT scan, T1-, T2-, and time-of-flight-weighted gadolinium contrast-enhanced MRI, and four-vessels, or six-vessels in case of cortical location, brain digital subtraction angiography (DSA). In cases of hemorrhagic onset characterized by the presence of an intracerebral hematoma, the indication for surgery was built upon a more general evidence-based management algorithm about intracerebral hemorrhages reported by our group [5]. Blood oxygenation level-dependent functional MRI was performed only in cases of elective AVMs involving eloquent areas. Based on size (S), involvement of eloquent area (E), and pattern of venous drainage (V), the selected grade III AVMs were further divided into four main types according to the parameters reported in Table 2. AVMs' volumes were calculated on DSA with the method reported by Pasqualin and colleagues [6]. As treatment strategy concerns, SM grade, angioarchitecture, evidence for flow-related or intranidal aneurysms, and stenosis of the straight sinus basically

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Table 1 Summary of patients' demographics, sites prevalence and clinical onset

Patients' demographics		***N. (±SD)***	
Average patients' age		*36.9 (±11.2) years*	
Male/female ratio		*2.8*	
Prevalence according to site		*N.*	
Infratentorial		*0*	
Supratentorial		*31*	
Main supratentorial site involved			
Site		***N. (%)***	***N. (%)***
Frontal lobe	*R*	–	*8 (25.8%)*
	L	*8 (25.8%)*	
Parietal lobe	*R*	*2 (6.4%)*	*4 (12.9%)*
	L	*2 (6.4%)*	
Central lobe	*R*	–	*6 (19.3%)*
	L	*6 (19.3%)*	
Occipital lobe	*R*	*4 (12.9%)*	*6 (19.3%)*
	L	*2 (6.4%)*	
Temporal lobe	*R*	*5 (16.1%)*	*6 (19.3%)*
	L	*1 (3.2%)*	
Insular cortex	*R*	–	–
	L		
Central core	*R*	–	*1 (3.3%)*
	L	*1 (thalamus) (3.2%)*	
Clinical onset		***N. (%)***	
Seizure		*6 (19.5%)*	
Focal deficits		*2 (6.5%)*	
Hemorrhage		*14 (45%)*	
Ischemic stroke		–	
Incidental		*9 (29%)*	
Average Admission WFNS Grade		***N. (±SD)***	
Hemorrhagic onset		*3.3 (±1.2)*	
Non-hemorrhagic onset		*1.2 (±0.5)*	

SD standard deviation, *WFNS* World Federation of Neurosurgical Societies Grading System

dictated the decision-making process within a multidisciplinary team of neurosurgeons and interventional neuroradiologists. The timeframe between the embolization sessions was also discussed on a case-by-case basis and mainly decided upon DSA findings. The effectiveness of the staged embolization was reported as a percentage ratio between the initial and the final post-embolization volume of the nidus.

During surgery, image guidance was used in all cases for both planning and intraoperative navigation, while neurophysiological monitoring was employed in eloquent area AVMs. A rigid 0° or 30°, 4 mm length endoscope was employed in all deep-seated or mesial AVMs treated using an inter-hemispheric approach to check for residuals at the final steps of surgery. Flow assessment techniques involved micro-Doppler ultrasound (MDU) (20 MHz System, Mizuho Medical Co., Ltd., Tokyo, Japan) since 2007, indocyanine green (ICG) video angiography (Flow 800 Infrared Module, OPMI Pentero 800, Zeiss, Oberkochen, Germany) since 2009, and fluorescein angiography (Yellow 560 Fluorescence Module, Kinevo 900, Zeiss, Oberkochen, Germany) since 2018. Operation time, blood loss, and admission WFNS grade were evaluated as variables in a comparison between a good, modified Ranking Scale (mRS) score <3, versus a bad mRS score >2, and overall outcome. A Mann-Whitney test for nonparametric statistical analysis was performed by means of GraphPad Prism software (GraphPad Software, La Jolla, California, USA), where the *P*-value was set at <0.05. All the embolization-related complications were described to assess the safety of the technique. The Overall outcome was reported as mRS [7] at a 6-month follow-up. Modified Ranking Scale scores of 0–2, 3, and 4–6 were assumed as good, moderate, and bad outcomes, respectively. The Overall radiological outcome was assessed based on the 6-month DSA.

Table 2 Typing, prevalence and overall outcome of grade III AVMs according to Spetzler-Martin grading system

SM classification parameters			Grade III typing		Prevalence	Overall outcome		
						mRS		
Size (cm)	Involvement of eloquent area	Type of venous drainage	Type	Class	*N.* (%)	0–2 *N* (%)	3 *N* (%)	4–6 *N* (%)
<3	Yes	Deep	I (S1E1V1)	Small-eloquent	12 (38.7%)	11 (91.7%)	1 (8.3%)	–
3–6	No	Deep	II (S2E0V1)	Medium-deep	12 (38.7%)	9 (75%)	3 (25%)	
3–6	Yes	Superficial	III (S2E1V0)	Medium-eloquent	6 (19.4%)	1 (16.7%)	5 (83.3%)	
>6	No	Superficial	IV (S3E0V0)	Large	1 (3.2%)	–	–	1 (100%)

SM Spetzler-Martin, *S* AVM size, *E* eloquent area; *V* venous drainage, *mRS* modified Rankin Scale score

Results

Prevalence of Grade III Types

The prevalence of type I (small-eloquent), medium-deep (type II), medium-eloquent (type III) and large (type IV) SM grade III AVMs was 38.7%, 38.7%, 19.4% and 3.2%, respectively (Table 2).

Technical Caveats of the Preoperative Functional Downgrading of AVMs

Thirty-one AVMs were embolized in 51 endovascular procedures. Only low-density Onyx (Onyx 18, 6% EVOH; Micro Therapeutics, Inc., eV3, Irvine, CA) was used as the embolic agent in the present series. Through a transarterial transfemoral approach, a flow-directed microcatheter (Marathon; eV3A) and a tapered microguidewire (Mirage; eV3) were advanced until the nidus. After a superselective catheterization of the main arterial feeders, a microcatheter was moved throughout the target feeders inside the nidus. While preferring the deep-seated parts, Onyx was injected with a flow rate of 0.1 mL/s by means of the "plug and push" technique [8]. The first session was always aimed to achieve the widest obliteration possible volume, stopping, however, after having reached the safest final possible result.

Effectiveness of the Staged Embolization

Average AVM volume at diagnosis was 19.7 (±3.8) mL versus a mean volume of 13.6 (±3) at the end of the last preoperative embolization session; the average obliteration rate was 29.6 (±14.6)%. The time window between the embolization sessions ranged between 10 and 15 days, whereas the mean number of the procedures performed per single patient was 1.6 (±0.6). The Average time between the last embolization and surgery session was 3.7 (±1.8) days. Intraoperatively, Onyx allowed for prompt identification of the nidus; also if initially racemose, it made it more compact and easier to dissect, and ultimately facilitated the hemostasis and the removal of the deepest parts of the malformation. No differences were found about operation time, blood loss, and WFNS grade comparing good versus bad outcome groups.

Safety of the Staged Embolization

Two mechanical and one hemodynamic endovascular complications were recorded during the embolization sessions; the mechanical ones both consisted of a catheter stuck, while a hemiparesis occurred in a single patient 8 h after the procedure. The estimated embolization-related morbidity rate was 3.2% with zero mortality.

Neurological and Angiographic Overall Outcome

At the 6-month follow-up, the overall outcome was as follows: mRS 0–2, mRS 3, and mRS > 4 in 77.5%, 19.3%, and 3.2% of the patients, respectively. Two patients (6.4%) had a small remnant, which underwent radiosurgery. As grade III typing concerns, the best outcome was achieved in small and medium-deep AVMs (Table 2).

Table 3 summarizes the overall data about staged embolization and surgery.

Illustrative Case

Case #1: SM Grade III AVM Involving the Right Primary Visual Cortex Secondary to a mild traumatic brain injury, a 48-year-old male was diagnosed with an incidental right occipital SM grade III AVM (Fig. 1). The Visual field test was normal. DSA of the right ICA and VA revealed two main arterial feeders from the distal right pericallosal artery (a) and the P3 segment of the right posterior cerebral artery (b and c). Small feeders also came from the distal left pericallosal artery (d). The huge nidus involved the right primary visual cortex and the venous phase showed two cortical veins draining into the posterior third of the superior sagittal sinus (e). A first Onyx embolization session was aimed to exclude the feeders from the right posterior cerebral artery (f and g), whereas a second session, performed after 12 days, allowed to occlude the feeders from the right pericallosal artery (h). Post-embolization preoperative DSA showed a rearrangement of the venous outflow (i) and MRI documented no ischemic complications (j). The final nidal volume was 11.3 mL and the estimated overall post-embolization rate was 49.7%.

The patients underwent surgery which consisted of the nidus excision by a posterior-interhemispheric approach with the patient in a prone position. Intraoperatively, a compact and very easy to dissect nidus was found (k–m). Furthermore, the blood loss was insignificant. Final ICG videoangiography in arterial (n) and venous (o) phase documented a normal filling of both neighboring arterial vessels and previously arterialized veins. No remnants were detected. Postoperative DSA confirmed a complete exclusion of the AVM (p–t) and the patient was discharged with no deficits on the fifth postoperative day.

Table 3 Data about staged embolization and surgery

Clinical onset	Average admission nidal volume (mL)	Onyx embolization			Average days between embolization and surgery	Average mRS
		Average procedures (*N.*)	Average overall post-embolization nidal volume (mL)	Average obliteration rate (%)		
Hemorrhagic onset	19 (±2.9)	1.5 (±2.4)	13.2 (±2.4)	29.1 (±16.1)	3.4 (±1.6)	0.7 (±1.1)
Non-hemorrhagic onset	20.2 (±4.3)	1.7 (±0.6)	13.9 (±3.3)	30.1 (±13.6)	4.1 (±1.9)	1.1 (±1.4)

mRS modified Rankin Scale score

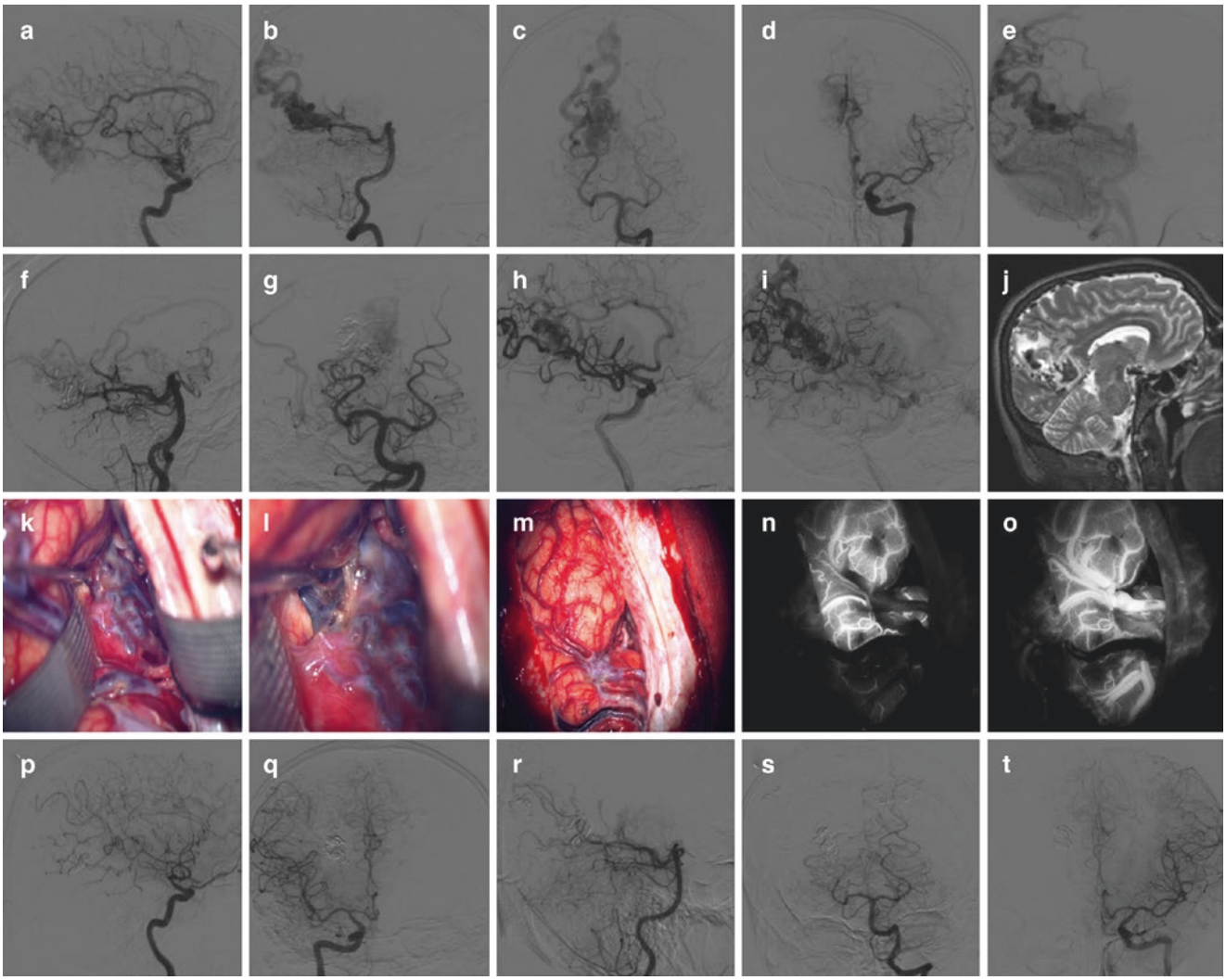

Fig. 1 DSA of the right ICA (**a**) and right VA in lateral (**b**) and anterior-posterior (**c**) projection revealing two main arterial feeders from the distal right pericallosal artery and the P3 segment of the right posterior cerebral artery. DSA of the left ICA (**d**). Right VA DSA in venous phase (**e**) showing the presence of two cortical veins draining into the posterior third of the superior sagittal sinus. DSA of the right VA in lateral (**f**) and anterior-posterior (**g**) projection after the first Onyx embolization session. DSA of the right ICA in lateral projection (**h**) after the second Onyx embolization session. (**i**) Right ICA DSA in venous phase showing the rearrangement and the slowing of the venous outflow. (**j**) Sagittal T2 weighted MRI revealing no ischemic complications after the second embolization session. (**k**, **l**) Intraoperative pictures during the right posterior inter-hemispheric approach showing the compactness of the nidus. (**m**) Intraoperative picture confirming the complete exclusion of the nidus at the final stage of surgery. Intraoperative ICG videoangiography in arterial (**n**) and venous (**o**) phase. Postoperative DSA of right ICA in lateral (**p**) and anterior-posterior (**q**) projection confirming the complete exclusion of the AVM. Postoperative DSA of the left VA in lateral (**r**) and anterior-posterior (**s**) projection (**t**) Postoperative DSA of the left ICA in anterior-posterior projection

Discussion

SM Grade III represents a heterogeneous group of brain AVMs concerning size, the involvement of eloquent areas, venous drainage, and, ultimately, angioarchitecture. Surgery has been reported as the option of choice for grade I and grade II malformations, but also for grade III ones [9]. Nevertheless, a paramount role of preoperative embolization has been now recognized and commonly implemented for the latter, being the elimination of the deeper feeders at the base of easier hemostasis and, lastly, reduced morbidity [9–11].

The results of the reported retrospective series fully confirm the effectiveness of the Onyx preoperative embolization before surgery of grade III AVMs. The good outcome observed especially in small-eloquent type I and medium-deep type II AVMs led to delineate these types as the best candidate for a preoperative endovascular AVM occlusion. Additionally, the overall results of the further two types are to be considered as other than free from additional and intrinsic angioarchitectural factors, eloquence first, which is undoubtedly related to higher morbidity [3, 4, 9, 12, 13]. echnically, the superselective microcatheterization of the feeders is the key starting point to achieve an effective but also safe preoperative embolization of the AVM through a detailed study of the shunts inside the nidus. Equally important is the recognition of the eventual peri-nidal angiogenesis in the form of a peripheric tenuous blush since it ought to be excluded from the embolization targets. The goal of the first session of the embolization should consist of a functional vascular downgrading of the AVM, having to be instead the subsequent sessions targeted to the deeper portion.

In our experience, the major advantages of the preoperative embolization came from the exclusion of the deeper arterial feeders, these being of utmost importance for affecting the morbidity and resectability of the larger malformations [1, 2].

Nevertheless, any endovascular overtreatment of the nidus ought to be avoided both because it is dangerous and because an excessive amount of embolic agent inside the nidus has been reported to interfere with the shrinking and mobilization of the nidus itself during surgery [1–4, 14–17].

Regarding the timeframe between the embolization sessions, an interval greater than 2 or 3 weeks at maximum should be avoided because of the well-known potential for the recruitment of new feeders. For the same reasons, surgery should be performed no later than 7 days from the last embolization. Within the present series, the implemented neurophysiological monitoring protocol, already reported by our group for vascular neurosurgery [18–24], was particularly useful also for those malformations located within eloquent areas. Equally helpful for checking for residuals at the final steps of surgery was endoscopic assistance in all deep-seated or mesial AVMs, the latter usually treated by means of an interhemispheric approach. The advantages of the endoscope-assisted technique for deep-seated AVMs are the same previously described by our group for the treatment of other pathologies characterized by the presence of blind spots [18, [25]. Lastly, an essential aspect of AVM surgery lies in constant microneurosurgical vascular training [26].

In conclusion, the results of the reported series confirm that preoperative staged embolization is a safe, feasible, and useful option in the treatment of both hemorrhagic and non-hemorrhagic SM Grade III AVMs.

A careful selection of patients as candidates for combined treatment, a detailed evaluation of the angioarchitecture, meticulous planning, and an effective and safe functional downgrading of the AVM, which should be based upon the key technical aspects reported in the present study, are all paramount factors the make surgery straightforward and, ultimately, to achieve the best outcome.

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References

1. Hurst RWBAKMJMMFES (1995) Deep central arteriovenous malformations of the brain: the role of endovascular treatment. J Neurosurg 82:190–195. https://doi.org/10.3171/jns.1995.82.2.0190
2. Vinuela FDGGG (1997) Contribution of interventional neuroradiology in the therapeutic management of brain arteriovenous malformations. J Stroke Cerebrovasc Dis 6:268–271
3. Yaşargil MG (1984) Microneurosurgery Volume III A. AVM of the Brain, History, Embryology, Pathological Considerations, Hemodynamics, Diagnostic Studies, Microsurgical Anatomy. vol v. 3,pt. 1. Georg Thieme
4. Yaşargil MG (1988) Microneurosurgery Vol. III B. AVM of the Brain, Clinical Considerations, General and Special Operative Techniques, Surgical Results, Nonoperated Cases, Cavernous and Venous Angiomas, Neuroanesthesia Thieme
5. Luzzi S, Elia A, Del Maestro M, Morotti A, Elbabaa SK, Cavallini A, Galzio R (2019) Indication, timing, and surgical treatment of spontaneous intracerebral hemorrhage: systematic review and proposal of a management algorithm. World Neurosurg. https://doi.org/10.1016/j.wneu.2019.01.016
6. Pasqualin ABGCFRLSR (1991) The relevance of anatomic and hemodynamic factors to a classification of cerebral arteriovenous malformations. Neurosurgery 28:370–379
7. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J (1988) Interobserver agreement for the assessment of handicap in stroke patients. Stroke 19:604–607
8. Siekmann R (2005) Basics and principles in the application of onyx LD liquid embolic system in the endovascular treatment of cerebral arteriovenous malformations. Interv Neuroradiol 11:131–140. https://doi.org/10.1177/15910199050110S117

9. Lawton MT (2003) Spetzler-Martin Grade III arteriovenous malformations: surgical results and a modification of the grading scale. Neurosurgery 52:740–748. discussion 748–749
10. Saatci IGSYKCHS (2011) Endovascular treatment of brain arteriovenous malformations with prolonged intranidal onyx injection technique: long-term results in 350 consecutive patients with completed endovascular treatment course. J Neurosurg 115:78–88. https://doi.org/10.3171/2011.2.JNS09830
11. Weber WKBSRJPLRKD (2007) Preoperative embolization of intracranial arteriovenous malformations with onyx. Neurosurgery 61:244–252.; discussion 252–244. https://doi.org/10.1227/01.NEU.0000255473.60505.84
12. Lawton MTKHMCEMBYWL (2010) A supplementary grading scale for selecting patients with brain arteriovenous malformations for surgery. Neurosurgery 66:702–713.; discussion 713. https://doi.org/10.1227/01.NEU.0000367555.16733.E1
13. Pandey PMMPHCDWEMCSDDHMLRPD (2012) Multimodality management of Spetzler-Martin grade III arteriovenous malformations. J Neurosurg 116:1279–1288. https://doi.org/10.3171/2012.3.JNS111575
14. Del Maestro M, Luzzi S, Gallieni M, Trovarelli D, Giordano AV, Gallucci M, Ricci A, Galzio R (2018) Surgical treatment of arteriovenous malformations: role of preoperative staged embolization. Acta Neurochir Suppl 129:109–113. https://doi.org/10.1007/978-3-319-73739-3_16
15. Luzzi S, Del Maestro M, Bongetta D, Zoia C, Giordano AV, Trovarelli D, Raysi Dehcordi S, Galzio RJ (2018) Onyx embolization before the surgical treatment of grade III Spetzler-Martin brain arteriovenous malformations: single-center experience and technical nuances. World Neurosurg 116:e340–e353. https://doi.org/10.1016/j.wneu.2018.04.203
16. Luzzi S, Del Maestro M, Elbabaa SK, Galzio R (2020) Letter to the Editor Regarding "One and Done: Multimodal Treatment of Pediatric Cerebral Arteriovenous Malformations in a Single Anesthesia Event". World Neurosurg 134:660. https://doi.org/10.1016/j.wneu.2019.09.166
17. Luzzi S, Del Maestro M, Galzio R (2019) Letter to the Editor. Preoperative embolization of brain arteriovenous malformations. J Neurosurg:1-2. https://doi.org/10.3171/2019.6.JNS191541
18. Gallieni M, Del Maestro M, Luzzi S, Trovarelli D, Ricci A, Galzio R (2018) Endoscope-assisted microneurosurgery for intracranial aneurysms: operative technique, reliability, and feasibility based on 14 years of personal experience. Acta Neurochir Suppl 129:19–24. https://doi.org/10.1007/978-3-319-73739-3_3
19. Luzzi S, Gallieni M, Del Maestro M, Trovarelli D, Ricci A, Galzio R (2018) Giant and very large intracranial aneurysms: surgical strategies and special issues. Acta Neurochir Suppl 129:25–31. https://doi.org/10.1007/978-3-319-73739-3_4
20. Ricci A, Di Vitantonio H, De Paulis D, Del Maestro M, Raysi SD, Murrone D, Luzzi S, Galzio RJ (2017) Cortical aneurysms of the middle cerebral artery: a review of the literature. Surg Neurol Int 8:117. https://doi.org/10.4103/sni.sni_50_17
21. Luzzi S, Gragnaniello C, Giotta Lucifero A, Del Maestro M, Galzio R (2020) Microneurosurgical management of giant intracranial aneurysms: Datasets of a twenty-year experience. Data Brief 33:106537. https://doi.org/10.1016/j.dib.2020.106537
22. Luzzi S, Gragnaniello C, Giotta Lucifero A, Del Maestro M, Galzio R (2020) Surgical Management of Giant Intracranial Aneurysms: Overall Results of a Large Series. World Neurosurg. https://doi.org/10.1016/j.wneu.2020.08.004
23. Luzzi S, Gragnaniello C, Giotta Lucifero A, Marasco S, Elsawaf Y, Del Maestro M, Elbabaa SK, Galzio R (2020) Anterolateral approach for subaxial vertebral artery decompression in the treatment of rotational occlusion syndrome: results of a personal series and technical note. Neurol Res:1-16. https://doi.org/10.1080/01616412.2020.1831303
24. Luzzi S, Gragnaniello C, Marasco S, Lucifero AG, Del Maestro M, Bellantoni G, Galzio R (2020) Subaxial Vertebral Artery Rotational Occlusion Syndrome: An Overview of Clinical Aspects, Diagnostic Work-Up, and Surgical Management. Asian Spine J. https://doi.org/10.31616/asj.2020.0275
25. Arnaout MM, Luzzi S, Galzio R, Aziz K (2020) Supraorbital keyhole approach: Pure endoscopic and endoscope-assisted perspective. Clin Neurol Neurosurg 189:105623. https://doi.org/10.1016/j.clineuro.2019.105623
26. Del Maestro M, Rampini Angela D, Mauramati S, Giotta Lucifero A, Bertino G, Occhini A, Benazzo M, Galzio R, Luzzi S (2020) Dye-Perfused Human Placenta for Vascular Microneurosurgery Training: Preparation Protocol and Validation Testing. World Neurosurg. https://doi.org/10.1016/j.wneu.2020.11.034