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Review Article

Transvenous Embolization for Brain Arteriovenous Malformations

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Brain arteriovenous malformations (bAVMs) are uncommon vascular lesions found in young individuals exhibiting diverse clinical manifestations ranging from asymptomatic to spontaneous intracranial hemorrhage, seizures, or headaches. Despite improvements in endovascular tools and methods, standalone transarterial embolization seldom achieves success rates surpassing 50%, even when employing ethylene vinyl alcohol copolymers. Transvenous embolization (TVE) emerges as a promising option, especially for bAVMs situated distally or inaccessible through arterial routes. Despite the possibility of achieving high angiographic cure rates, concerns regarding hemorrhagic complications persist, limiting its adoption. This review article outlines the indications and methodology of TVE, discusses complications, and highlights the essential expertise needed for the safe execution of TVE along with strategies to mitigate associated risks. Clinical results reveal promising outcomes in terms of obliteration rates and favorable neurological results, although challenges persist, particularly regarding device accessibility and risk management. Despite these challenges, TVE remains a valuable alternative for managing bAVMs, particularly for cases resistant to surgical intervention, emphasizing the significance of careful patient selection and procedural expertise.

Keywords brain arteriovenous malformation, curative embolization, endovascular embolization

Introduction

Brain arteriovenous malformations (bAVMs) are uncommon vascular lesions, varying from asymptomatic to causing intracranial hemorrhage, seizures, or headaches, particularly in younger individuals.[1] Treatment options include medical management, microsurgical resection, stereotactic radiosurgery, endovascular embolization, or a combination of these methods.[2] Endovascular embolization is often used alongside microsurgical resection or stereotactic radiosurgery as a component of multimodal therapy for bAVMs.[3–5]

With advancements in endovascular tools and methodologies, endovascular embolization aimed at curing bAVMs has gained significant attention in numerous treatment centers.[6] However, standalone transarterial embolization rarely achieves success rates exceeding 50%, even with the use of ethylene vinyl alcohol copolymers (EVOH).[7–9]

Transvenous embolization (TVE) provides distinct advantages over the transarterial method, especially in scenarios involving highly distal nidus locations or complex arterial anatomy.[10] The earliest account of TVE with a precipitating embolic agent dates back to 2003 during the ABC WIN seminar in Val d'Isère in France by Dr. Houdak, followed in 2005 by Dr. Houdart and Dr. Chapot at the same gathering. This approach shows potential for achieving a high rate of angiographic cure and addressing otherwise untreatable bAVMs.[11,12] However, concerns about the risk of hemorrhagic complications during or after TVE often result in a reluctance to utilize these methods.

This review article outlines the indication and method of TVE, examines complications—including hemorrhagic ones—and discusses the necessary expertise required to conduct TVE safely and strategies to minimize related risks.

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Indications

For TVE, treatment results have mainly been published by Dr. Mounayer's team in Limoges, France, and Dr. Chapot's team in Essen, Germany. In a 2015 paper from Dr. Mounayer's group in the *Journal of Neurosurgery*, the following indications for TVE were emphasized: (1) rupture cases; (2) high Spetzler Martin grade; (3) lesions located in deep or vital areas such as basal ganglia, paraventricular areas, choroidal and deep white matter components, and eloquent cortical areas; (4) cases with challenging access through the transarterial method; (5) presence of a single drainage vein; (6) relatively small nidus or remaining nidus; and (7) cases deemed challenging to treat at other medical centers.[13] The same group also documented unruptured cases and lower Spetzler Martin grade cases after the initial paper.[14] In a 2018 publication by Dr. Chapot's team in the *Journal of NeuroInterventional Surgery*, the indications are outlined as follows: (1) failure of transarterial cure, (2) AVM <3 cm, and (3) the existence of a single outflow vein.[11] These indications largely coincided with those outlined by Dr. Mounayer's team. Furthermore, a paper presented to AJNR from China in 2019 was found to have nearly identical indications.[15] These results suggest a common agreement among various research teams concerning the indications for TVE treatment. However, as transvenous techniques have advanced and accumulated more expertise, the indications have broadened to include certain bAVMs with nidus size larger than 3 cm and drained by two or more veins.[12]

Procedures

The TVE approach reported by Dr. Mounayer's and Dr. Chapot's teams exhibits numerous similarities, but the technique of retrograde EVOH injection from the venous side varies. The size and type of instruments utilized in the treatment vary accordingly. The former uses a simple embolization method known as the plug-and-push technique, with a relatively high injection speed compared to antegrade arterial injection,[12,16] whereas the latter utilizes a pressure cooker technique.[11,17] In the pressure cooker technique,[11,17] at least two microcatheters are positioned on the venous side, requiring a larger guiding catheter on the venous side accordingly. The following is a summarized description of the method based on their reports.[11–13]

Anesthesia

The procedures were carried out under general anesthesia, according to reports from both groups.

Approaches

TVEs employ both arterial and venous approaches to the nidus. The arterial microcatheter is strategically positioned in the arterial feeder for two main reasons: first, to enable a superselective angiogram of all feeders, providing comprehensive visualization of the bAVM structure, optimizing nidus visualization and accurate venous microcatheter placement; and second, to serve as a safety precaution, allowing embolic agent administration via the arterial route if necessary, particularly in cases of intraoperative complications or incomplete nidus occlusion following venous injection.[11,12]

The road map function aided in accessing the internal jugular vein on the side of the lesion. A short sheath was inserted into the internal jugular vein, and a guiding catheter was utilized to access the straight or the superior sagittal sinus, positioning the distal end of the catheter at the base of the bAVM's primary draining vein. The size of the guiding catheter depends on the method the physician chooses. The main reasons for accessing the venous approach from the jugular vein are (1) because it is closer to the target and (2) if the microcatheter employed for embolization from the venous side cannot be removed, cut at the jugular vein will lead to a shorter residual indwelling in the body. Dr. Mounayer's team utilizes mainly non-detachable-tip microcatheters for TVE, so they are typically cut in the jugular vein, but no additional postoperative anticoagulation is utilized.[12]

Retrograde catheterization of the main outflow vein

The plug-and-push technique, utilizing only one microcatheter, is simple and involves the advancement of a single microcatheter into the outflow vein as usual (**Fig. 1A**), while the pressure cooker technique necessitates additional procedures.[11,17] A retrograde micro-catheterization of the main outflow vein must be obtained with two microcatheters: a first detachable-tip microcatheter to inject EVOH and a second microcatheter for plug creation. The first detachable-tip microcatheter was positioned in the primary outflow vein at the merging point of the primary veins. The second microcatheter was advanced alongside the first microcatheter based on the principle of the sheeping technique until its tip reached the same level (**Fig. 1B**).[18] Transarterial superselective angiography or elective 3D rotational angiography from the arterial feeder aids in achieving the optimal position of the venous catheter.

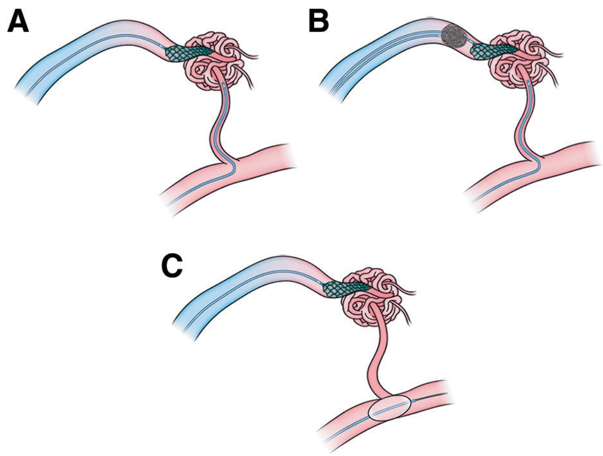

Fig. 1 Illustrations of the transvenous embolization. (**A**) Retrograde simple EVOH injection.[13] Illustration depicting the transvenous embolization procedure utilizing retrograde simple EVOH injection from a single microcatheter in the drainage vein. A second microcatheter is placed in the feeding artery to enable superselective angiography and act as a safety measure, facilitating embolic agent administration via the arterial route if necessary. (**B**) Transvenous retrograde pressure cooker technique.[11] Illustration demonstrating retrograde EVOH injection using the retrograde pressure cooker technique. Two microcatheters are positioned on the venous side: one for EVOH injection and the other for plug creation using coils and cyanoacrylate glue. Arterial microcatheter placement is shown to serve the roles described above. (**C**) Selective temporary flow arrest during transvenous endovascular embolization.[21] Illustration depicting selective temporary flow arrest during transvenous embolization using hyper-compliant balloons intra-arterially. This technique reduces intra-nidal pressure during retrograde simple EVOH injection from a single microcatheter in the drainage vein. EVOH, ethylene vinyl alcohol copolymer

Control of the intranidal pressure

Reducing the intranidal inflow could provide beneficial conditions for the retrograde, transvenous progression of the liquid agent into the nidus. Massoud and Hademenos previously outlined the advantages of hypotension during transvenous retrograde embolization.[19,20] During the retrograde embolization, arterial blood pressure was maintained at a maximum of 120/80 mmHg in Dr. Mounayer's team.[12,13] They also noted the effectiveness of temporal occlusion of arterial feeders utilizing the super-compliant balloon to reduce the intranidal pressure more efficiently than usual systemic blood pressure control (**Fig. 1C**).[21] Dr. Chapot's team employed strict control, aiming to keep systolic blood pressure below 70–80 mmHg.[11]

Coiling on the venous side

The transvenous pressure cooker technique utilizes a transvenous plug of coils and cyanoacrylate glue, followed by TVE (**Fig. 1B**). Coiling is conducted via a second microcatheter. For veins <3 mm in diameter, a Magic microcatheter (Balt Extrusion, Montmorency, France) was employed as the second catheter to deliver flow coils (SPIF Flow Coils; Balt Extrusion) along the detachment tip of the other. For larger veins, a microcatheter suitable for delivering electrically detachable coils was employed. Coiling was achieved through the second microcatheter, backward from the tip of the first detachable-tip microcatheter on a 20 mm segment of length, aiming to obtain the highest possible density.[11]

Retrograde injection of EVOH

In the transvenous pressure cooker method, after coiling, EVOH copolymer (Onyx 18; Medtronic, Minneapolis, MN, USA, and later Squid-12, Emboflu, Gland, Switzerland) was injected through the first microcatheter. Injection was paused as soon as EVOH reached the coils and repeated several times until the flow in the vein was almost interrupted. At that stage, 50% acrylic glue was introduced into the coils via the second microcatheter until a complete filling of this venous segment was achieved. Subsequently, additional EVOH was retrogradely injected until the entire AVM was filled.[11] The AVM was deemed cured once the final cast of embolic material matched with the pre-interventional angiographic aspect on the same working projection. In Dr. Mounayer's team, the EVOH injection was conducted slowly but at a higher rate than the transarterial injection. They limited the reflux length on the venous side up to 3 cm to prevent venous infarction.[12] In case of doubtful residual micro-shunts, a selective catheterization with a microcatheter placed in the arterial side was achieved to identify potential feeders with a remaining flow to the AVM, followed by transarterial embolization if necessary.

Postoperative control of blood pressure

Systolic blood pressure was maintained at 20 mmHg below normal pressure for 24 h.[11,12]

Clinical Results

Obliteration rate

Complete obliteration was found in 49/51 patients (96%) after a single session in Dr. Chapot's series.[11] The anatomic cure rate was reported in 52/57 (91.2%) bAVMs in Dr. Mounayer's series.[22] Even in small clinical series, complete AVM nidus obliteration was demonstrated in 16/19 (84%) patients with technically feasible AVMs immediately after embolization.[15] A systemic review by Batista et al. of 16 publications focusing on TVE for bAVM yielded an overall complete occlusion rate of 91% (95% confidence interval [CI]: 88%, 94%; I^2=43%, p=0.04), showing a high level of technical success with TVE.[23)]

Hemorrhagic complication

One concern regarding embolization from the venous side is hemorrhagic complications. This is because many vascular neurosurgeons have been trained during their residency that the main draining vein is not sacrificed until all incoming feeders have been severed and the nidus has been completely isolated from the surrounding parenchyma to avoid massive bleeding.[24)] Another concern is the possibility of the microcatheter penetrating the vein wall during the approach due to the delicate nature of vein walls, unlike arteries. Dr. Chapot's team documented postoperative intracranial hemorrhage occurred in 5.9% (3/51) of the patients, including one case attributed to perforation from retrograde venous micronavigation.[11)] This rate is consistent with the hemorrhagic complication rate in the systemic review at 6% (95% CI: 3–8; I^2=8%, p=0.37).[23)] However, Dr. Mounayer's series demonstrated a higher hemorrhagic complication rate of 17.5%, in which the number of the drainer was identified as the independent predictor of hemorrhagic complications (odds ratio, 8.7; 95% CI: 2.2–58.2, p = 0.006).[22)] TVE could be safely conducted for the AVMs with a single draining vein. However, expanding the indication of TVE to the AVM with two or more draining veins should be prevented at this time.

Clinical outcomes

In a recent systematic review, favorable outcomes (modified Rankin Scale [mRS] 0-2) were attained in 89% (95% CI: 82–96) of cases utilizing a random-effects model, though there was some variability in the results (I^2=63%, p <0.01).[23)] Remarkably, about 60% of bAVMs showed the higher Spetzler Martin grade III to V, known to carry a high risk of poor patients' clinical results with surgical removal.[2)]

Current Situation in Japan

Currently, the use of TVE in Japan seems to be relatively limited. One contributing factor is the perceived risk linked with embolization alone: a randomized trial of unruptured brain arteriovenous malformations (ARUBA) finding showed a high rate of stroke and death within 1 month, reaching 15.4% in the group treated solely with embolization.[25)] Similarly, results from the treatment of brain AVMs study (TOBAS) study show that 14% of patients who underwent curative embolization, mainly through the transarterial approach, had an mRS score of 2 or higher or died, with only 30% achieving complete embolization.[7)]

Another obstacle lies in the limitations of available devices. The detachable-tip microcatheter, widely used in Europe and the United States, is appropriate for EVOH embolization of bAVMs but is not accessible in Japan. Another concern is the EVOH copolymer, Squid12, which has an even lower viscosity, is considered more suitable for TVE than Onyx 18 but is also unavailable in Japan.[26)]

Despite these challenges, bAVMs with hemorrhage not suitable for surgical intervention may be considered for TVE due to their relatively safe profile and high embolization success rates, especially in cases exhibiting anatomical characteristics mentioned in the "indications" section above.

Conclusion

In conclusion, TVE provides a promising method for treating bAVMs, particularly in cases where the transarterial approach may be limited or ineffective. The indications for TVE have been well documented, demonstrating a common consensus among various research teams regarding its suitability. Despite concerns about hemorrhagic complications, TVE has shown high rates of angiographic cure and favorable clinical outcomes in numerous cases. Technological advancements have enhanced the safety and efficacy of TVE, although challenges such as limited device availability persist, particularly in regions like Japan. Nevertheless, TVE remains a valuable option for addressing bAVMs, providing a relatively safe profile and high success rates, especially in cases with specific anatomical characteristics. Continued research and development in this field are crucial to further refine and expand the utility of TVE in the treatment of bAVMs.

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