Transvenous embolization of brain arteriovenous malformations: a review of techniques, indications, and outcomes

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Endovascular embolization of brain arteriovenous malformations (AVMs) is conventionally performed from a transarterial approach. Transarterial AVM embolization can be a standalone treatment or, more commonly, used as a neoadjuvant therapy prior to microsurgery or stereotactic radiosurgery. In contrast to the transarterial approach, curative embolization of AVMs may be more readily achieved from a transvenous approach. Transvenous embolization is considered a salvage therapy in contemporary AVM management. Proposed indications for this approach include a small (diameter < 3 cm) and compact AVM nidus, deep AVM location, hemorrhagic presentation, single draining vein, lack of an accessible arterial pedicle, exclusive arterial supply by perforators, and en passage feeding arteries. Available studies of transvenous AVM embolization in the literature have reported high complete obliteration rates, with reasonably low complication rates. However, evaluating the efficacy and safety of this approach is challenging due to the limited number of published cases. In this review the authors describe the technical considerations, indications, and outcomes of transvenous AVM embolization.

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the common theme of all interventions. Premature venous occlusion or ligation can result in nidus engorgement and disastrous hemorrhagic complications. Serial disconnection of an AVM’s arterial supply prior to the final ligation of the draining vein is a fundamental principle of AVM resection.\textsuperscript{5,51} Similarly, progressive AVM devascularization via occlusion of arterial feeders and nidal penetration by liquid embolizes can be achieved with endovascular embolization, which is conventionally performed from a transarterial approach.\textsuperscript{9} Despite its challenges in achieving adequate nidal penetration without early compromise of venous drainage, transvenous embolization has recently been introduced as a potentially curative intervention for carefully selected AVMs. In this review, we describe the techniques, indications, and outcomes of transvenous AVM embolization.

**Technical Considerations**

The rising popularity of transvenous AVM embolization stems from successful transvenous treatment paradigms for dural arteriovenous fistulas (DAVFs). Pioneering work on transvenous embolization of transverse-sigmoid sinus DAVFs and carotid-cavernous fistulas by Halbach et al. described transvenous navigation of microcatheters into the sites of venous drainage, with delivery of coils or liquid embolizes to achieve DAVF obliteration.\textsuperscript{21,22} However, the transvenous approach for AVMs faced significant challenges because the fistulous connections in AVM nidi are predominantly between arterioles and venules. Because these foci of arteriovenous shunting are more distally located and have more tortuous courses than dural venous sinuses (i.e., for transvenous embolization of DAVFs), they are typically more difficult to access from a transvenous route.\textsuperscript{24}

A model for transvenous AVM embolization was first conceptualized by Massoud and Hademenos.\textsuperscript{37} The authors described the transvenous retrograde nidus sclerotherapy under controlled hypotension (TRENSH) technique using temporary systemic hypotension with or without temporary occlusion of the main arterial feeders, allowing for a more thorough permeation of an AVM nidus than could otherwise be achieved with the transarterial route, while avoiding ischemic complications that may be encountered with embolization through arterial feeders. Subsequently, Massoud et al. showed that induced systemic hypotension may decrease intranidal pressure, and thus reduce the risk of iatrogenic nidal hemorrhage using electrical network analyses that modeled transvenous AVM embolization.\textsuperscript{38} This was followed by a study by Massoud using a carotid-jugular fistula-type swine AVM model that demonstrated decreased arterial feeder pressure, increased extent of retrograde nidus contrast filling, and concurrent contrast emptying through a greater number of draining veins with systemic hypotension and temporary arterial feeder occlusion.\textsuperscript{36} This experimental model formed the basis for subsequent clinical studies of transvenous AVM embolization.

Transvenous microcatheter navigation presents unique challenges due to the variability and tortuosity of the venous system that can be encountered. Although the arterialized veins found in AVMs have relatively thicker walls, the fragility of cortical veins unrelated to the AVM pose a greater risk of perforation than transarterial navigation. Recent advancements in the compliance and flexibility of microcatheters and microguidewires have improved the safety of transvenous catheterization and navigation.\textsuperscript{8} Despite this, defining and understanding the venous anatomy remains crucial to successfully traversing the venous system during the transvenous approach to AVMs.

In cases of difficult venous anatomy, a compliant balloon can be used in the dural venous sinus as a proximal buttress to facilitate microguidewire navigation and microcatheter tracking.\textsuperscript{40} However, navigation of two microcatheters in the venous system is not always feasible, especially in the tortuous and smaller-caliber cortical veins. Control angiograms performed through an arterial microcatheter and guide catheter are essential to providing the roadmap for navigation through the venous system, and superselective injections through the arterial microcatheter allow for better characterization of the nidus and optimal positioning of the venous microcatheter. Furthermore, embolic agents can be injected through the arterial microcatheter if necessary, in instances of inprocedural AVM rupture or residual nidus following transvenous embolization.\textsuperscript{40} Previously, transjugular access using a triaxial system was routinely used for transvenous AVM embolization. Transjugular access allows a microcatheter that has been entrapped in the embolic cast to be cut at the neck, to avoid induction of a cardiac arrhythmia by a retained microcatheter traversing the heart, as would be the case with transfemoral venous access.\textsuperscript{34} Newer microcatheters with detachable tips allow for safer microcatheter removal after embolization, thereby improving the feasibility of transfemoral access for transvenous AVM embolization.\textsuperscript{23}

Preservation of the venous outflow until complete nidal obliteration remains the primary challenge of the transvenous approach, as premature venous occlusion can result in nidus engorgement, elevated intranidal pressure, and ensuing AVM rupture. The TRENSH technique, via decreased intranidal pressure gradient, allows for retrograde filling of the nidus and closure of arteriovenous shunting with minimal reflux. In addition, positioning the venous microcatheter as close as possible to the nidus reduces the risk of venous reflux. The neurointerventionalist’s knowledge and understanding of an AVM’s venous drainage pattern is essential to avoiding premature venous drainage occlusion. AVMs with multiple draining veins are considered safer for the transvenous approach because reflux of excess embolysate into accessory venous outflow channels avoids premature occlusion of the vein accessed by the microcatheter.\textsuperscript{4,20} However, the TRENSH technique was only tested in a single draining vein model, and controlling embolysate permeation of the nidus may be easier in AVMs with a single draining vein.\textsuperscript{4}

As demonstrated in the TRENSH technique, induced hypotension, systemically and locally at the AVM nidus, is essential to overcoming the feeding arterial pressure by the embolysate and its retrograde penetration of the nidus. Although the balance between the extent of feasible hypotension and optimal retrograde nidus penetration by embolysate remains unknown, the transnidal pressure...
more recently, precipitating hydrophobic injectable liquid AVMs include N-butyl cyanoacrylate (NBCA), ethylene vinyl alcohol copolymer (Onyx, ev3 Neurovascular), and more recently, precipitating hydrophobic injectable liquid (PHIL). Compared to NBCA, Onyx laminates along the vessel wall, and is both less adhesive and more cohesive. Due to the rapidity of its polymerization, NBCA is not suitable for transvenous embolization, as immediate occlusion of the draining vein can be disastrous. The slower polymerization rate and cohesive nature of Onyx allows it to be injected over a period of several minutes to over an hour for a more controlled embolization. In contrast to the transarterial approach, Onyx injection time in the draining vein should be as short as possible to form the initial plug, and the time interval to resume injection is also shorter (approximately 20 seconds) compared to arterial embolizations. Coils may be deployed upstream to the draining vein prior to Onyx injection to limit reflux of the embolysate, premature draining vein occlusion, and pulmonary embolism. Additionally, balloon inflation at the juncture of the draining vein and dural venous sinus during Onyx injection may increase the venous resistance and improve its retrograde penetration.

Indications

The indications for transvenous embolization of AVMs have yet to be rigorously assessed and validated. Most of the indications proposed in the literature suggest the transvenous approach as a salvage therapy. Relative indications for the transvenous approach included a small and compact AVM nidus (< 3 cm in maximum diameter), deep-seated AVMs with a high operative risk, and ruptured AVMs. Although AVMs with multiple draining veins may have built-in mechanisms to allow egress of refluxed embolysate, those with single draining veins are often considered more favorable for the transvenous approach, as nodal penetration is more easily achieved. Additional indications for the transvenous approach are AVMs without safe arterial access, including those with no clearly defined arterial pedicle, tiny perforating arteries, and en passage feeding arteries. Inaccessible nodal remnants identifiable by a persistent draining vein after transarterial embolization, incomplete microsurgery, or failed stereotactic radiosurgery are also reasonable candidates for transvenous embolization. Lastly, the transvenous approach may be used in combination with transarterial embolization in cases for which the goal is endovascular cure.

We illustrate the case of a 38-year-old man with a history of intraventricular hemorrhage from a ruptured, small tectal AVM that was treated using Onyx via the transvenous approach (Fig. 1). The AVM was supplied by perforating branches arising from the right superior cerebellar artery, and the venous drainage was exclusively deep through the right internal cerebral vein (ICV). The final angiogram following transvenous embolization demonstrated complete obliteration of the AVM nidus, with parent artery preservation. There were no procedural complications. The patient remained clinically stable and was discharged 3 days later.

Outcomes

Table 1 summarizes the baseline characteristics and outcomes of transvenous AVM embolization reported in the literature. The literature review included 13 studies, comprising 69 patients with 70 AVMs that were treated with transvenous embolization. The treated AVMs ranged between < 1 and 5 cm in maximum diameter, and the Spetzler-Martin grade (reported in 68 of 70 cases) was I in 7 AVMs (10%), II in 25 (37%), III in 24 (35%), and IV in 12 (18%). Embolic agents used included Onyx, PHIL, coils, and Glubran (GEM Srl). The majority of the AVMs had a single draining vein (81%) and were ruptured (71%). Most of these AVMs were supplied by small arterial feeders that were challenging to selectively catheterize. Complete AVM obliteration was achieved in 93% of cases for which the intent of treatment was curative embolization. The complication rate was modest (4.3%). However, it is important to note that these cases were highly selected, based on angiographic features, for transvenous embolization. With the relatively modest number of transvenous AVM embolization cases reported in the literature, one should note that the majority of the cases were derived from studies by Mendes et al. Therefore, given the aforementioned indications, the reported outcomes of the transvenous approach may not be generalizable to all AVMs.

In the largest case series to date, comprising 40 patients who underwent transvenous embolization of 41 AVMs, Mendes et al. reported an obliteration rate of 92.6%. Hemorrhagic presentation was noted in 67.5% of patients, and all patients underwent transvenous embolization with an intent to cure. A single draining vein was noted in 75% of AVMs, and 54% had deep venous drainage. A combination of Onyx, PHIL, and coils were used. A single transvenous embolization session was performed in 56% of cases, transarterial embolization prior to transvenous intervention was performed in 27%, and combined transarterial and transvenous embolization was performed in 17%. There were 2 complications (5%), including 1 case of intra procedural venous rupture and another case of hemorrhagic transformation of a perinidal venous infarct. No procedure-related mortality was observed. Prior to the first embolization session, 75% of patients had no significant clinical impairment (modified Rankin Scale [mRS])

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score < 3), and significant disability (mRS score ≥ 3) was observed in 1 patient (2.5%) at 6-month follow-up.

Complications

Among the cases reported in the literature, 3 complications associated with transvenous AVM embolization have been reported, yielding an overall complication rate of 4.3%. Trivelato et al. reported a case of transient right cranial nerve V1 hypoesthesia with right lateral pontine surface edema on MRI following transvenous embolization of an 8-mm right middle cerebellar peduncle AVM supplied by a duplicated right superior cerebellar artery and right internal auditory artery arising from the basilar trunk.54 Various techniques, including coil deployment upstream to the draining vein prior to Onyx injection and balloon inflation at the draining vein–dural venous sinus juncture during Onyx injection, may increase venous resistance and prevent excessive reflux.40,56 Mendes et al. described 2 complications in their experience of treating 41 AVMs in 40 patients with transvenous embolization.40 One patient suffered subarachnoid hemorrhage due to microcatheter perforation during navigation through a cortical vein. There was no clinical sequela associated with the venous perforation. The other patient developed a venous infarct due to venous outflow occlusion, which resulted in transient hemiparesis. The deficit improved to the patient’s preoperative baseline at 6-month follow-up. This case again underscores the risk of venous reflux and premature draining vein occlusion–associated transvenous AVM embolization. Therefore, in addition to understanding an AVM’s angioarchitecture and careful selection of appropriate lesions, optimizing the microcatheter position in relation to the draining vein and minimizing venous reflux are essential to safely employing this technique.

Conclusions

For a highly selected subset of AVMs, endovascular cure can be achieved with transvenous embolization in the
TABLE 1. Characteristics and outcomes of AVMs treated with transvenous embolization

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Pts</th>
<th>Mean Age (yrs)</th>
<th>Females (%)</th>
<th>SM Grade</th>
<th>Size Range (cm)</th>
<th>Embolic Agent</th>
<th>SDV (%)</th>
<th>Prior Hemorrhage (%)</th>
<th>Prior Tx (%)</th>
<th>Obliteration (%)</th>
<th>Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Konan et al., 1999</td>
<td>1</td>
<td>35</td>
<td>0/1 (0)</td>
<td>NR</td>
<td>NR</td>
<td>Coils</td>
<td>0/1 (0)</td>
<td>0/1 (0)</td>
<td>1/1 (100)</td>
<td>0/1 (0)*</td>
<td>0/1 (0)</td>
</tr>
<tr>
<td>Benabu et al., 2010</td>
<td>1</td>
<td>13</td>
<td>0/1 (0)</td>
<td>IV</td>
<td>4</td>
<td>Coils</td>
<td>1/1 (100)</td>
<td>0/1 (0)</td>
<td>1/1 (100)</td>
<td>0/1 (0)*</td>
<td>0/1 (0)</td>
</tr>
<tr>
<td>Nguyen et al., 2010</td>
<td>1</td>
<td>50</td>
<td>0/1 (0)</td>
<td>II</td>
<td>&lt;1</td>
<td>Onyx</td>
<td>1/1 (100)</td>
<td>1/1 (0)</td>
<td>0/1 (0)</td>
<td>1/1 (100)</td>
<td>0/1 (0)</td>
</tr>
<tr>
<td>Kessler et al., 2011</td>
<td>5</td>
<td>41.8</td>
<td>2/5 (40)</td>
<td>III: 3, IV: 2</td>
<td>1–5</td>
<td>Onyx</td>
<td>3/5 (40)</td>
<td>4/5 (80)</td>
<td>2/5 (40)</td>
<td>4/5 (80)</td>
<td>0/5 (0)</td>
</tr>
<tr>
<td>Consoli et al., 2013</td>
<td>5</td>
<td>33.4</td>
<td>5/5 (100)</td>
<td>II: 2, III: 3</td>
<td>1.5–3</td>
<td>Onyx</td>
<td>4/5 (80)</td>
<td>5/5 (100)</td>
<td>1/5 (20)</td>
<td>5/5 (100)</td>
<td>0/5 (0)</td>
</tr>
<tr>
<td>Martinez-Galdamez et al., 2014</td>
<td>1</td>
<td>45</td>
<td>1/1 (100)</td>
<td>II</td>
<td>0.9</td>
<td>Onyx</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
<td>0/1 (0)</td>
</tr>
<tr>
<td>Pereira et al., 2013</td>
<td>1</td>
<td>31</td>
<td>0/1 (0)</td>
<td>II</td>
<td>2</td>
<td>Squid 18</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
<td>0/1 (0)</td>
<td>1/1 (100)</td>
<td>0/1 (0)</td>
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<tr>
<td>Trivelato et al., 2014</td>
<td>1</td>
<td>56</td>
<td>0/1 (0)</td>
<td>II</td>
<td>0.8</td>
<td>Onyx</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
<td>0/1 (0)</td>
<td>1/1 (100)</td>
<td>1/1 (100)*</td>
</tr>
<tr>
<td>Orlov et al., 2015</td>
<td>1</td>
<td>41</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td>Renieri et al., 2015</td>
<td>4</td>
<td>11</td>
<td>2/4 (50)</td>
<td>I: 3, II: 1</td>
<td>&lt;1–2</td>
<td>Onyx (venous), Glubran (arterial)</td>
<td>3/4 (75)</td>
<td>1/4 (25)</td>
<td>0/4 (0)</td>
<td>4/4 (100)</td>
<td>0/1 (0)</td>
</tr>
<tr>
<td>Mendes et al., 2016</td>
<td>7</td>
<td>13.6</td>
<td>4/7 (57)</td>
<td>II: 5, III: 2</td>
<td>1.3–3</td>
<td>Onyx (venous), Glubran (arterial)</td>
<td>NR</td>
<td>7/7 (100)</td>
<td>3/7 (43)</td>
<td>7/7 (100)</td>
<td>0/7 (0)</td>
</tr>
<tr>
<td>Zhang et al., 2017</td>
<td>1</td>
<td>58</td>
<td>1/1 (100)</td>
<td>III</td>
<td>2</td>
<td>Onyx, coils</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
<td>0/1 (0)</td>
<td>1/1 (100)</td>
<td>0/1 (0)</td>
</tr>
<tr>
<td>Mendes et al., 2017</td>
<td>40‡</td>
<td>37.7</td>
<td>22/40 (55)</td>
<td>I: 4, II: 13, III: 15, IV: 9</td>
<td>1–4</td>
<td>Coils, Onyx, PHIL</td>
<td>31/41 (75)</td>
<td>27/40 (67.5)</td>
<td>NR</td>
<td>38/41 (92.6)</td>
<td>2/40 (5)$</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>—</td>
<td>37/68 (54)</td>
<td>I: 7, II: 25, III: 24, IV: 12</td>
<td>&lt;1–5</td>
<td>Coils, Onyx, PHIL, Glubran</td>
<td>50/62 (80.6)</td>
<td>49/69 (71)</td>
<td>10/29 (34.4)</td>
<td>63/68 (92.6)$</td>
<td>3/69 (4.3)</td>
</tr>
</tbody>
</table>

NR = not reported; Pts = patients; SDV = single draining vein; SM = Spetzler-Martin; Tx = treatment.
* Not intended for AVM obliteration.
† The patient developed right cranial nerve V1 hypoesthesia, and MRI showed edema involving the right lateral surface of the pons that was not present preoperatively. The patient's symptoms resolved after 4 weeks, and follow-up MRI showed complete resolution of the edema.
‡ Forty patients with 41 AVMs.
§ One patient with a ruptured cortical AVM had subarachnoid hemorrhage secondary to microcatheter perforation during navigation through a cortical vein, without clinical consequences. The other patient with an unruptured Rolandic AVM had a venous infarct due to venous outflow occlusion, which resulted in transient hemiparesis; this neurological deficit improved to the patient's preoperative baseline at 6-month follow-up.
¶ Includes only AVMs treated with intention for cure.
majority of cases. Currently, the transvenous approach is considered an un proven salvage therapy in the contemporary management of AVMs. Relative indications for trans venous embolization include a small and compact AVM nidus, deep AVM location, hemorrhagic presentation, single draining vein, lack of a navigable arterial feeder, and inaccessible nidal remnant. Currently, the risk-to-benefit profile of transvenous AVM embolization is incompletely defined due to the modest number of reported cases in the literature and limited posttreatment follow-up. Additionally, the long-term rates of nidal recanalization with this technique are poorly understood. Therefore, future studies comprising larger cohorts are needed to refine the indications and delineate the outcomes of transvenous emboliza tion for AVMs.

References

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Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: Kalani. Acquisition of data: Chen, Norat. Analysis and interpretation of data: Chen, Norat. Drafting the article: Chen, Norat. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Kalani. Statistical analysis: Chen. Administrative/technical/material support: Kalani. Study supervision: Kalani.

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